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     (FILE 'HOME' ENTERED AT 10:04:29 ON 13 NOV 2008)

     FILE 'REGISTRY' ENTERED AT 10:04:56 ON 13 NOV 2008
L1             STRUCTURE UPLOADED
L2               7 S L1
L3             212 S L1 SSS FUL
L4             198 S L3 AND CAPLUS/LC
L5              14 S L3 NOT L4

     FILE 'CAPLUS' ENTERED AT 10:06:12 ON 13 NOV 2008
L6              65 S L3
L7             ANALYZE L6 1- RN HIT :     198 TERMS

     FILE 'REGISTRY' ENTERED AT 10:06:43 ON 13 NOV 2008
L8               1 S 188844-34-0/RN
L9               1 S 172705-89-4/RN
L10              1 S 188645-44-5/RN
L11              1 S 155877-83-1/RN
L12         138712 S 6-6-7/SZ
L13          34137 S 5-6-6-7/SZ
L14          15955 S 6-6-6-7/SZ
L15           2422 S 6-6-7-7/SZ
L16             22 S L3 AND L12
L17              0 S L3 AND L13
L18            182 S L3 AND L14
L19              0 S L3 AND L15
L20            204 S L16 OR L18
L21              8 S L3 NOT L20
L22            191 S L20 AND CAPLUS/LC
L23             13 S L20 NOT L22

     FILE 'CAPLUS' ENTERED AT 10:10:56 ON 13 NOV 2008
L24             57 S L20
L25             49 S L24 NOT (2008/SO OR 2007/SO OR 2006/SO OR 2005/SO)

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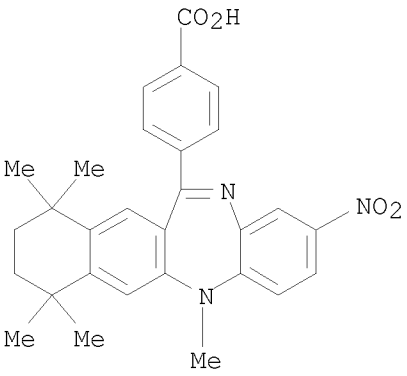
L25 ANSWER 1 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1229267 CAPLUS
TITLE: The transcription factors Nur77 and retinoid X receptors participate in amphetamine-induced locomotor activities
AUTHOR(S): Bourhis, Emmanuelle; Maheux, Jerome; Paquet, Brigitte; Kagechika, Hiroyuki; Shudo, Koichi; Rompre, Pierre-Paul; Rouillard, Claude; Levesque, Daniel
CORPORATE SOURCE: Faculty of Pharmacy, University of Montreal Pavillon Jean-Coutu, Montreal, QC, H3C 3J7, Can.
SOURCE: Psychopharmacology (Berlin, Germany) No pp. yet given
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The major substrate underlying amphetamine (AMPH)-induced locomotor activity is associated with dopamine forebrain circuits. Brain regions associated with AMPH-induced locomotor activity express high levels of retinoid receptors. However, the role of these transcription factors in dopamine-mediated effects remains poorly understood. Two nuclear receptor families, the retinoic acid receptors (RAR) and the retinoid X receptors (RXR), transduce retinoic acid signal. RARs are specifically involved in retinoid signaling, whereas RXRs also participate in other signaling pathways as partners for other nuclear receptors such as Nur77, an orphan member of the nuclear receptor family expresses in dopamine system. To explore the role of retinoid receptors and Nur77 in AMPH-induced locomotor activity, we administered selective retinoid receptor drugs in combination with AMPH in adult wild-type and Nur77-deficient mice. At a low dose, AMPH similarly increased ambulatory activity in wild-type and Nur77-deficient mice, while it did not alter non-ambulatory activity. At a high dose, AMPH did not alter ambulatory activity anymore, while non-ambulatory activity strongly increased in wild-type mice. Nur77-deficient mice still displayed a higher ambulatory activity with no change in non-ambulatory activity. HX531, a synthetic RXR antagonist, blocks AMPH-induced ambulatory activity, whereas RAR drugs tested remained without effect. Interestingly, the effect of HX531 was abolished in Nur77-deficient mice, suggesting that this orphan nuclear receptor is essential for the action of the RXR drug. This study shows that RXR and Nur77 participate in AMPH-induced locomotor activity and prompts for further investigations on the role of Nur77 and RXR in addiction and reward-related behaviors.
IT 188844-34-0, HX531
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transcription factors Nur77 and retinoid X receptors participation in amphetamine-induced locomotor activities in relation to dopamine and drug addiction)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)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NO2
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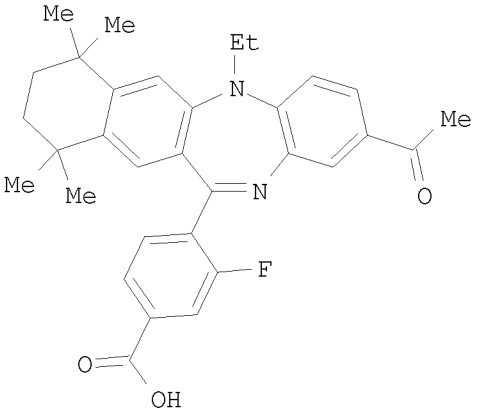
Me
Me
Me

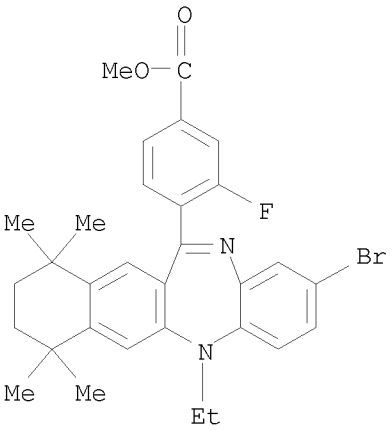
L25 ANSWER 2 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1144614 CAPLUS
TITLE: A Practical Synthesis of a Diazepinylbenzoic Acid, a Retinoid X Receptor Antagonist
AUTHOR(S): Jiang, Xinglong; Lee, George T.; Prasad, Kapa; Repic, Oljan
CORPORATE SOURCE: Process Research and Development, Novartis Pharmaceuticals Corporation, East Hanover, NJ, 07936, USA
SOURCE: Organic Process Research & Development ACS ASAP
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



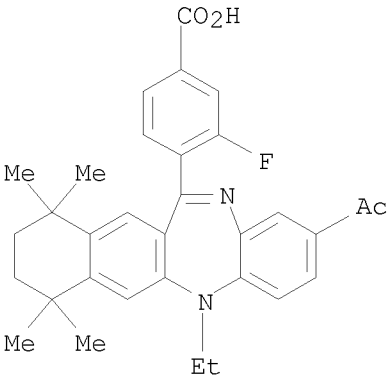
I

AB An optimized convergent synthetic route for the preparation of retinoid X receptor (RXR) antagonist I in an overall yield of 35% is described. The formation of the benzodiazepine was achieved in 85% yield using POCl3 in toluene. The drug substance I was obtained by treatment of aryl bromide with vinyl Bu ether in the presence of palladium acetate, DPPP, and cesium carbonate. This one-pot operation incorporating three chemical transformations (i.e., Heck reaction, hydrolysis of vinyl ether, and hydrolysis of ester) was achieved in 85% yield.

IT 1068616-19-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diazepinylbenzoic acid via Pd-catalyzed one-pot Heck reaction of aryl bromide with vinyl Bu ether, and hydrolysis of vinyl ether and ester)
RN 1068616-19-2 CAPLUS
CN Benzoic acid, 4-(2-bromo-5-ethyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-3-fluoro-, methyl ester (CA INDEX NAME)



IT 777074-39-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(target compound; preparation of diazepinylbenzoic acid via Pd-catalyzed one-pot Heck reaction of aryl bromide with vinyl Bu ether, and hydrolysis of vinyl ether and ester)
RN 777074-39-2 CAPLUS
CN Benzoic acid, 4-(2-acetyl-5-ethyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-3-fluoro- (CA INDEX NAME)

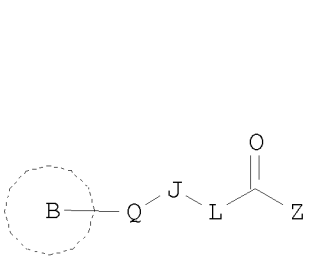


REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

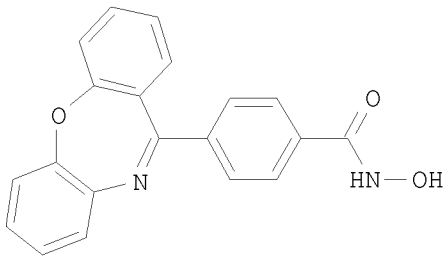
L25 ANSWER 3 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:556979 CAPLUS
DOCUMENT NUMBER: 148:538314
TITLE: Preparation of tricyclic hydroxamic acids as inhibitors of histone deacetylase
INVENTOR(S): Shapiro, Gideon; Moncuso, John; Pierre, Tessier; Leit, Silvana; Deziel, Robert; David, Smil; Richard, Chesworth; Chantigny, Yves Andre; Patrick, Beaulieu
PATENT ASSIGNEE(S): Methygene Inc., Can.; En Vivo Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 405pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008055068	A2	20080508	WO 2007-US82668	20071026
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080207590	A1	20080828	US 2007-925151	20071026
PRIORITY APPLN. INFO.:			US 2006-863347P	P 20061028
			US 2007-884287P	P 20070110

OTHER SOURCE(S): MARPAT 148:538314
GI



I



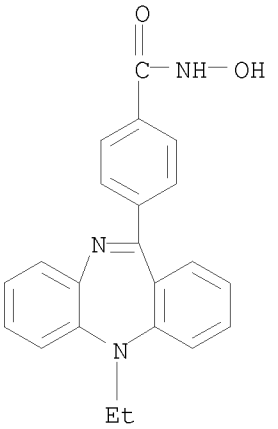
II

AB The title compds. I [Z = N(R1)OR2, H; L = a bond, N(OR2); when L = N(OR2), Z = H; when Z = H, L = N(OR2); R1, R2 = H, alkyl, aryl, etc.; J = a bond, :CH-, alkyl, alkyl(heteroalkyl)alkyl, etc.; Q = diazepine, pyrrolidine, diazabicyclo[3.3.1]nonane, etc.; B = dibenzo[b,f][1,4]oxazepine, benzo[b]pyrido[2,3-e][1,4]diazepine, benzo[f]thieno[2,3-b][1,4]oxazepine,

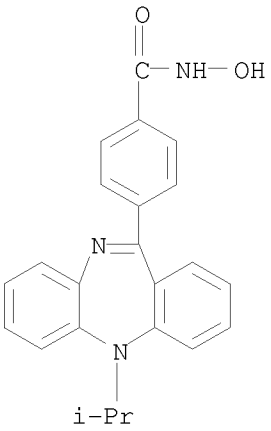
etc.;], useful for the inhibition of histone deacetylase, were prepared E.g., a 3-step synthesis of II, starting from 10,11-dihydrodibenz[b,f][1,4]oxazepin-11-one, was given. All exemplified compds. I have an IC50 of ≤ 10 μM against one of more of HDAC-1 through HDAC-11 (data for representative compds. I were given). Pharmaceutical composition comprising the compound I and methods of treating polyglutamine (polyQ) expansion diseases such as Huntington's disease, are disclosed.

IT 1024007-44-0P 1024007-85-9P 1024007-88-2P
1024008-01-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic hydroxamic acids as inhibitors of histone deacetylase)

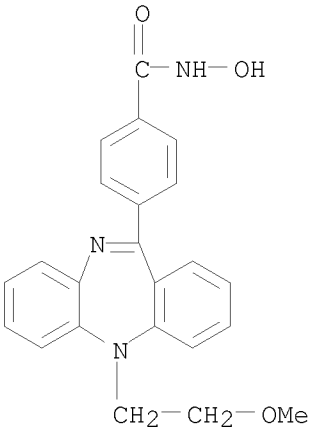
RN 1024007-44-0 CAPLUS
CN Benzamide, 4-(5-ethyl-5H-dibenzo[b,e][1,4]diazepin-11-yl)-N-hydroxy- (CA INDEX NAME)



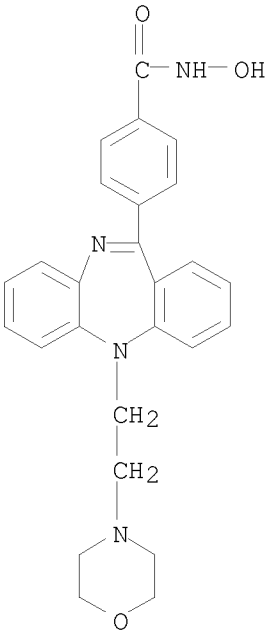
RN 1024007-85-9 CAPLUS
CN Benzamide, N-hydroxy-4-[5-(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



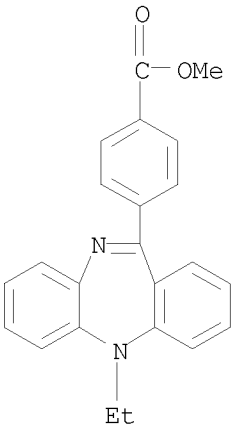
RN 1024007-88-2 CAPLUS
CN Benzamide, N-hydroxy-4-[5-(2-methoxyethyl)-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



RN 1024008-01-2 CAPLUS
CN Benzamide, N-hydroxy-4-[5-[2-(4-morpholinyl)ethyl]-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



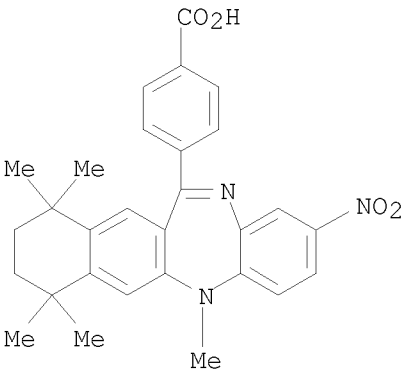
IT 1024010-79-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tricyclic hydroxamic acids as inhibitors of histone deacetylase)
RN 1024010-79-4 CAPLUS
CN Benzoic acid, 4-(5-ethyl-5H-dibenzo[b,e][1,4]diazepin-11-yl)-, methyl ester (CA INDEX NAME)



L25 ANSWER 4 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:283293 CAPLUS
DOCUMENT NUMBER: 146:288505
TITLE: Remedy for osteoporosis with the use of retinoid x receptor-related compound
INVENTOR(S): Udagawa, Nobuyuki; Nakamura, Midori; Kagechika, Hiroyuki
PATENT ASSIGNEE(S): Matsumoto Dental University, Japan
SOURCE: PCT Int. Appl., 24pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007029642	A1	20070315	WO 2006-JP317454	20060904
WO 2007029642	A9	20070510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
JP 2007070281	A	20070322	JP 2005-258480	20050906
PRIORITY APPLN. INFO.:			JP 2005-258480 A	20050906

AB It is intended to provide a novel remedy for osteoporosis. Use is made of HX531 which is synthesized as an antagonist to retinoid X receptor and has an activity of inhibiting the differentiation of adipocytes. The remedy can be used in an oral dosage form containing HX531 as the active ingredient.
IT 188844-34-0, HX531
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinoid receptor antagonists as remedy for osteoporosis)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

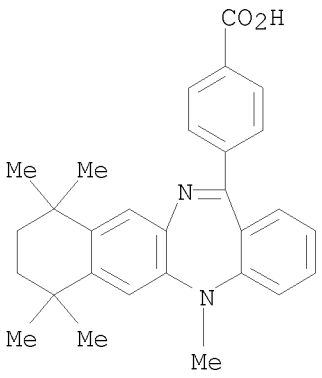
L25 ANSWER 5 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:230699 CAPLUS
DOCUMENT NUMBER: 146:266788
TITLE: Medicament having neovascularization promoting action
INVENTOR(S): Nagai, Ryozo; Manabe, Ichiro; Shindo, Takayuki; Iwata, Hiroshi; Shudo, Koichi; Kagechika, Hiroyuki
PATENT ASSIGNEE(S): Research Foundation Itsuu Laboratory, Japan
SOURCE: U.S. Pat. Appl. Publ., 7pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070049579	A1	20070301	US 2006-366454	20060303
PRIORITY APPLN. INFO.:			US 2005-658175P P	20050304

AB A medicament having a neovascularization promoting action, which comprises a retinoid antagonist such as 4-(5H-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethylbenzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)benzoic acid as an active ingredient and is useful for prophylactic and/or therapeutic treatment of ischemic diseases and wounds.

IT 155877-83-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicament having neovascularization promoting action)

RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)

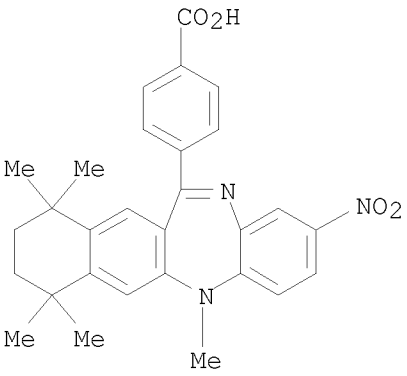


L25 ANSWER 6 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:818071 CAPLUS
DOCUMENT NUMBER: 145:224886
TITLE: Remedy for neurogenic pain
INVENTOR(S): Tanabe, Tsutomu
PATENT ASSIGNEE(S): Japan Science and Technology Agency, Japan; Tokyo Medical and Dental University
SOURCE: PCT Int. Appl., 23pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006085686	A1	20060817	WO 2006-JP302778	20060210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
JP 2007332031	A	20071227	JP 2005-33900	20050210
PRIORITY APPLN. INFO.:			JP 2005-33900 A	20050210

AB It is intended to provide a remedy for neurogenic pain exerting an excellent therapeutic effect on neurogenic pain which is an intractable disease. More specifically speaking, it is intended to provide a remedy for neurogenic pain which contains, as the active ingredient, a PPAR antagonist (in particular, a PPARγ-selective antagonist such as 2-chloro-5-nitro-N-phenylbenzamide), a medicinal composition for treating neurogenic pain which contains, as the active ingredient, a PPAR antagonist, a method of treating neurogenic pain with the use of a PPAR antagonist and so on.

IT 188844-34-0, HX531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PPAR antagonists as remedies for neurogenic pain)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

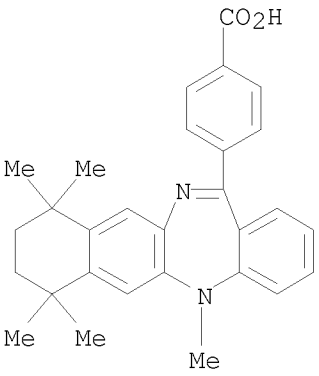
L25 ANSWER 7 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1282118 CAPLUS
DOCUMENT NUMBER: 144:17169
TITLE: Inducers and inhibitors for gut-homing of T-cells, intestinal immunostimulants, manufacture of T-cells with enhanced homing ability, homing-preventing functional foods, and drug screening method
INVENTOR(S): Iwata, Makoto; Song, Shih Rong
PATENT ASSIGNEE(S): Mitsubishi Chemical Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005336062	A	20051208	JP 2004-153548	20040524

PRIORITY APPLN. INFO.: JP 2004-153548 20040524

AB The inducers for homing of T-cells to intestinal tissues contain retinoic acid (RA) receptor-activating substances or naive T-cells cultured in the presence of the substances. The intestinal immunostimulants contain RA receptor-activating substances. The inhibitors for homing of T-cells to intestinal tissues contain RA receptor antagonists or naive T-cells cultured in the presence of RA receptor antagonists. T-cells with enhanced ability of gut-homing are manufactured by culturing naive T-cells, separated from living bodies, in the presence of RA receptor-activating substances. The functional foods for prevention of gut-homing of T-cells contain reduced amts. of vitamin A. The inhibitors for gut-homing of T-cells or the intestinal immunostimulants are screened by culturing naive T-cells in the presence of test substances and selecting the test substances on the basis of the amts. of expression of components required for homing of the cells to intestinal tissues. Thus, all-trans RA (at ≥0.1 nM) increased the expression of α4β7-integrin and decreased the expression of L-selectin (CD62L) in cultured naive CD4+ T-cells isolated from mice. All-trans RA (at 10-8 M) induced the expression of mRNA of CCR9 gene in the cultured T-cells.

IT 155877-83-1, LE 135
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinoic acid receptor agonists/antagonists or cultured T-cells for control of gut-homing of T-cells, immunostimulants, functional foods, and drug screening method)
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)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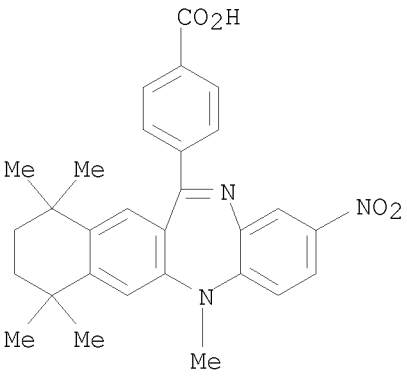
L25 ANSWER 8 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1233307 CAPLUS
DOCUMENT NUMBER: 143:432401
TITLE: Novel RXR antagonists enhance transactivation of PPARγ and ST 13 preadipocyte differentiation
AUTHOR(S): Sato, M.; Sugawara, A.; Egawa, N.; Yajima, Y.; Kato, H.; Kagechika, H.
CORPORATE SOURCE: Tokyo Metropolitan Institute for Medical Science, Bunkyo-ku, Tokyo, 113-8613, Japan
SOURCE: International Congress of Endocrinology, Proceedings, 12th, Lisbon, Portugal, Aug. 31-Sept. 4, 2004 (2004), E831C0752/547-E831C0752/551. Monduzzi Editore: Bologna, Italy.
CODEN: 69HNUT; ISBN: 88-7587-072-1
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English
AB Retinoid X receptor (RXR) belong a nuclear receptor super family that functions as a ligand-activated transcription factor. We identified novel RXR ligands PA 451, PA 452 and HX 531 are pure competitive RXR antagonists. Although these RXR antagonists function as antagonists toward RXR:RAR heterodimer, they function as agonists toward RXR:PPARγ (peroxisome proliferator activated receptor). This agonistic activity of RXR antagonists was also demonstrated against endogenous RXR:PPARγ. Simultaneous treatment with RXR antagonists and PPARγ agonist enhance the transactivation of PPARγ response element (PPRE) via RXR:PPARγ and induction of ST 13 preadipocyte differentiation. We father demonstrate that amphipathic activity appeared in these RXR antagonists is depend on the structure of ligand binding domain of heterodimer partner.
IT 188844-34-0, HX 531
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(RXR antagonists enhancement of PPARγ receptor transactivation and ST 13 preadipocyte differentiation)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1220224 CAPLUS
DOCUMENT NUMBER: 143:473581
TITLE: Novel substitution variants of nuclear receptors and their use in a dual switch inducible system for regulation of gene expression
INVENTOR(S): Palli, Subba Reddy; Kumar, Mohan Basavaraju
PATENT ASSIGNEE(S): Rheogene,Inc., USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005108617	A2	20051117	WO 2005-US15089	20050502
WO 2005108617	A3	20060209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050266457	A1	20051201	US 2005-118855	20050429
AU 2005241051	A1	20051117	AU 2005-241051	20050502
CA 2563521	A1	20051117	CA 2005-2563521	20050502
EP 1744619	A2	20070124	EP 2005-743351	20050502
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1964622	A	20070516	CN 2005-80018417	20050502
BR 2005010498	A	20071120	BR 2005-10498	20050502
JP 2008505616	T	20080228	JP 2007-511069	20050502
MX 2006PA12594	A	20061215	MX 2006-PA12594	20061030
KR 2007016157	A	20070207	KR 2006-725112	20061129
IN 2006DN07237	A	20070824	IN 2006-DN7237	20061130
US 20080145935	A1	20080619	US 2007-841464	20070820
US 20080216184	A1	20080904	US 2007-841631	20070820

PRIORITY APPLN. INFO.:		
US 2004-567294P	P	20040430
US 2004-609424P	P	20040913
US 2005-118855	A	20050429
WO 2005-US15089	W	20050502

OTHER SOURCE(S): MARPAT 143:473581

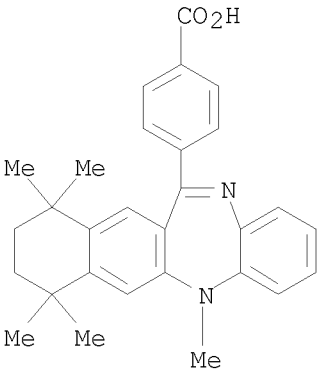
AB Novel substitution mutant of nuclear receptors, specifically Group H nuclear receptors, that show improved ligand responsiveness that can be used to modulate gene expression in a host cell for applications such as gene therapy, large scale production of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic organisms. In particular, one gene expression cassette is inducibly regulated by a steroid ligand and the other gene

expression cassette is inducibly regulated by a non-steroid ligand. Specific embodiments of the invention provide ecdysone receptor ligand-binding domains fused to the DNA-binding domains of GAL4 or LexA, and the ligand-binding domains of retinoid X receptor or ultraspiracle protein fused to the VP16 transactivation domain. A series of substitution mutants of insect ecdysteroid receptors were prepared by standard PCR mutagenesis and tested for their responsiveness to ecdysteroid induction of reporter gene expression in the dual switch system. Variants that showed increased responsiveness to the ecdysteroids with decreased responsiveness to non-steroid ligands were identified. Variants showed increased responsiveness to both classes of effectors, or to nonsteroids but not ecdysteroids, were also identified.

IT 172705-89-4D, HX600, thiadiazepine analogs
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulation of receptor function and gene expression by; novel substitution variants of nuclear receptors and their use in dual switch inducible system for regulation of gene expression)

RN 172705-89-4 CAPLUS

CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



L25 ANSWER 10 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:982601 CAPLUS
DOCUMENT NUMBER: 143:260373
TITLE: Retinoid antagonists for promoting neovascularization
INVENTOR(S): Nagai, Ryozo; Manabe, Ichiro; Shindo, Takayuki; Iwata, Hiroshi; Sudo, Koichi; Kagechika, Hiroyuki
PATENT ASSIGNEE(S): Research Foundation Itsuu Laboratory, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

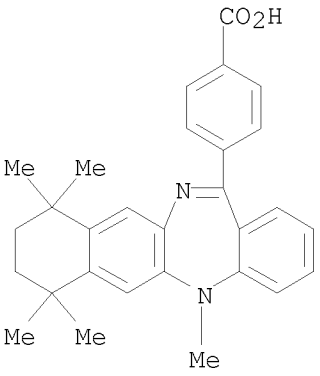
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005239631	A	20050908	JP 2004-51218	20040226

PRIORITY APPLN. INFO.: JP 2004-51218 20040226

AB Claimed are retinoid antagonists with neovascularization-promoting activities for the treatment of ischemic heart diseases, such as myocardial infarction, angina pectoris, leg-obstructive arteriosclerosis, Buerger's disease, and cerebral infarction. The retinoid antagonists include 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)benzoic acid (LE 135) and salts thereof.

IT 155877-83-1, LE 135
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinoid antagonists for promoting neovascularization)

RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



L25 ANSWER 11 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:451232 CAPLUS
DOCUMENT NUMBER: 143:19954
TITLE: Methods for inhibiting cell growth
INVENTOR(S): Zhao, Yi; Chandraratna, Roshantha A.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046726	A2	20050526	WO 2004-US37881	20041112
WO 2005046726	A3	20051208		

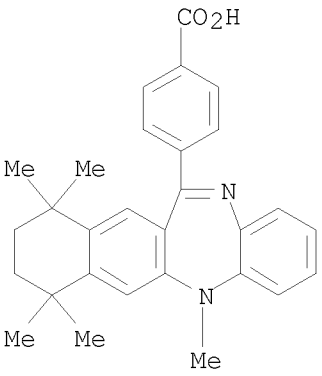
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-519528P P 20031112
US 2004-564807P P 20040422

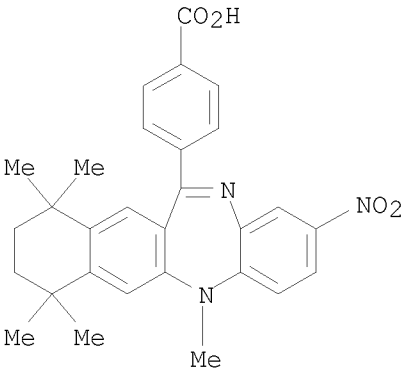
AB Cell growth is inhibited and/or cell death is induced in a cell by administering an RXR (retinoid X receptor) agonist and an inhibitor of casein kinase 1 α. A cell or a tissue can be screened for enhanced susceptibility to cell death or interference with cell growth. Conditions characterized by uncontrolled cell growth or proliferation, such as a cancer, can be treated with inhibitors of casein kinase 1 α.

IT 172705-89-4 188844-34-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for inhibiting cell growth using retinoid X receptor agonists and casein kinase 1 α inhibitors in relation to drug screening)

RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



L25 ANSWER 12 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:220022 CAPLUS
DOCUMENT NUMBER: 142:294308
TITLE: Expansion of renewable stem cell populations using modulators of phosphatidylinositol 3-kinase, and therapeutic applications
INVENTOR(S): Peled, Tony; Grynspan, Frida
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 106 pp., Cont.-in-part of Appl. No. PCT/IL03/00681.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050054103	A1	20050310	US 2004-795215	20040304
WO 2003078567	A2	20030925	WO 2003-IL235	20030318
WO 2003078567	A3	20040610		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004016731	A2	20040226	WO 2003-IL681	20030817
WO 2004016731	A3	20040910		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005200679	A1	20050324	AU 2005-200679	20050216
ZA 2005007161	A	20060830	ZA 2005-7161	20050906

PRIORITY APPLN. INFO.:		
US 2003-452545P	P	20030307
WO 2003-IL235	A2	20030318
WO 2003-IL681	A2	20030817
US 2002-364590P	P	20020318
US 2002-404137P	P	20020819
US 2002-404145P	P	20020819
IL 2002-152904	A	20021117
WO 2003-IL62	A	20030123
WO 2003-IL64	A	20030126
AU 2003-250519	A3	20030817

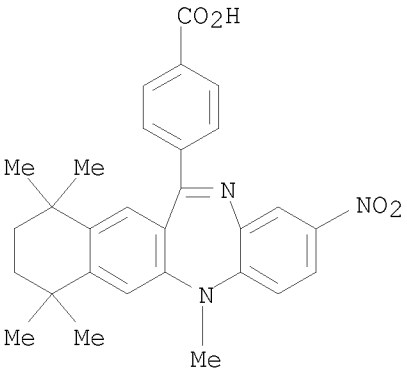
AB The present invention relates to methods of expansion of renewable stem cells, to expanded populations of renewable stem cells and to their uses.

In particular, ex-vivo and/or in-vivo stem cell expansion is achieved according to the present invention by downregulation of a phosphatidylinositol 3-kinase (PI 3-kinase) signaling pathway, either at the protein level via PI 3-kinase inhibitors, such as, wortmannin and LY294002, or at the expression level via genetic engineering techniques, such as small interfering RNA (siRNA), ribozyme, and antisense techniques. RAR and RXR receptors antagonists were prepared and used in ex-vivo hematopoietic progenitor cell expansion. The present invention further relates to therapeutic applications in which these methods and/or the expanded stem cells populations obtained thereby are utilized.

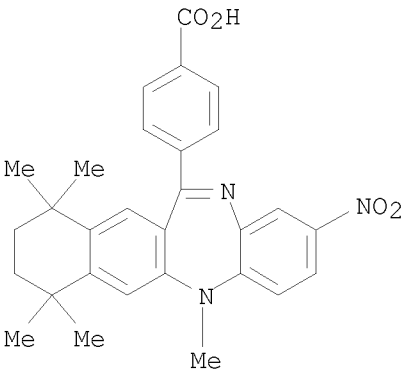
IT 188844-34-0P, HX531
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of RAR+RXR antagonists for use in cell expansion; expansion of renewable stem cell populations using modulators of phosphatidylinositol 3-kinase, and therapeutic applications)

RN 188844-34-0 CAPLUS

CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



L25 ANSWER 13 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:39489 CAPLUS
DOCUMENT NUMBER: 142:254766
TITLE: Monitoring ligand-mediated nuclear receptor-coregulator interactions by noncovalent mass spectrometry
AUTHOR(S): Sanglier, Sarah; Bourguet, William; Germain, Pierre; Chavant, Virginie; Moras, Dino; Gronemeyer, Hinrich; Potier, Noelle; Van Dorsselaer, Alain
CORPORATE SOURCE: Laboratoire de Spectrometrie de Masse Bio-Organique, CNRS UMR 7509, ECPM, Strasbourg, Fr.
SOURCE: European Journal of Biochemistry (2004), 271(23/24), 4958-4967
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retinoid receptors are ligand-dependent transcription factors belonging to the nuclear receptor superfamily. Retinoic acid (RARα, β, γ) and retinoid X (RXRα, β, γ) receptors mediate the retinoid/rexinoid signal to the transcriptional machineries by interacting at the first level with coactivators or corepressors, which leads to the recruitment of enzymically active noncovalent complexes at target gene promoters. It has been shown that the interaction of corepressors with nuclear receptors involves conserved LXXI/HIXXXXI/L consensus sequences termed corepressor nuclear receptor (CoRNR) boxes. Here we describe the use of nondenaturing electrospray ionization mass spectrometry (ESI-MS) to determine the characteristics of CoRNR box peptide binding to the ligand binding domains of the RARα-RXRα heterodimer. The stability of the RARα-RXRα-CoRNR ternary complexes was monitored in the presence of different types of agonists or antagonists for the two receptors, including inverse agonists. These results show unambiguously the differential impact of distinct retinoids on corepressor binding. We show that ESI-MS is a powerful technique that complements classical methods and allows one to: (a) obtain direct evidence for the formation of noncovalent NR complexes; (b) determine ligand binding stoichiometries and (c) monitor ligand effects on these complexes.
IT 188844-34-0, HX 531
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ESI-MS monitoring of ligand-mediated retinoid nuclear receptor-coregulator interactions)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 14 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:878381 CAPLUS
DOCUMENT NUMBER: 141:350204
TITLE: Preparation of 11-phenyldibenzodiazepine derivatives as RXR-antagonists
INVENTOR(S): Sakaki, Junichi; Konishi, Kazuhide; Kishida, Masashi; Kimura, Masaaki; Uchiyama, Hidefumi; Mitani, Hironobu
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004089916	A1	20041021	WO 2004-EP3806		20040408
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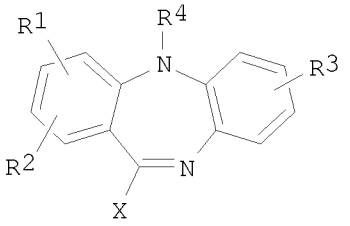
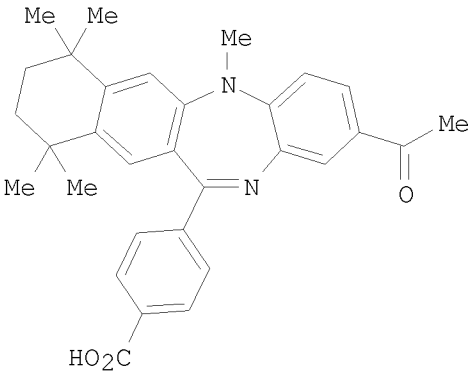
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004228357	A1	20041021	AU 2004-228357		20040408
AU 2004228357	B2	20080911			
CA 2521337	A1	20041021	CA 2004-2521337		20040408
EP 1618096	A1	20060125	EP 2004-726490		20040408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004009365	A	20060425	BR 2004-9365		20040408
CN 1771232	A	20060510	CN 2004-80009666		20040408
JP 2006522767	T	20061005	JP 2006-505085		20040408
IN 2005CN02560	A	20070831	IN 2005-CN2560		20051006
MX 2005PA10861	A	20051214	MX 2005-PA10861		20051007
US 20070043029	A1	20070222	US 2006-550776		20060620
PRIORITY APPLN. INFO.:			GB 2003-8335	A	20030410
			WO 2004-EP3806	W	20040408

OTHER SOURCE(S): CASREACT 141:350204; MARPAT 141:350204
GI



I



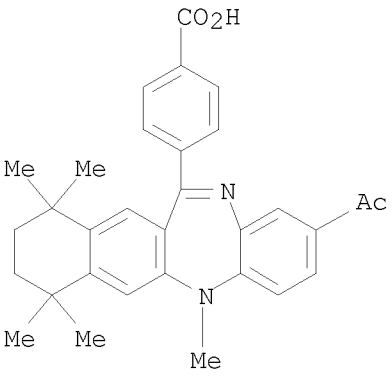
II

AB Title compds. I [R1-2 = H, alkyl, etc.; R3 = CN, acyl, H, etc.; R4 = alk(en/yn)yl, alkanoyl, etc.; X = substituted phenyl] are prepared For instance, II is prepared in 6 steps from (2-nitrophenyl)(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)amine (prior art). I are exhibit RXR-antagonist efficacy and are useful in the treatment of diabetes, complication of diabetes such as retinopathy, nephropathy, neuropathy, hyperlipidemia, obesity, dyslipidemia, and osteoporosis.

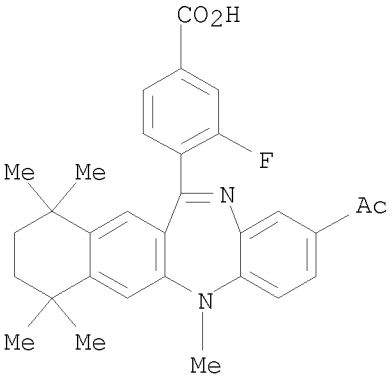
IT 777074-35-8P 777074-36-9P 777074-37-0P
777074-38-1P 777074-39-2P 777074-40-5P
777074-41-6P 777074-42-7P 777074-43-8P
777074-44-9P 777074-45-0P 777074-46-1P
777074-47-2P 777074-48-3P 777074-49-4P
777074-50-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 11-phenyldibenzodiazepine derivs. as RXR-antagonists for treatment of, e.g., diabetes)

RN 777074-35-8 CAPLUS

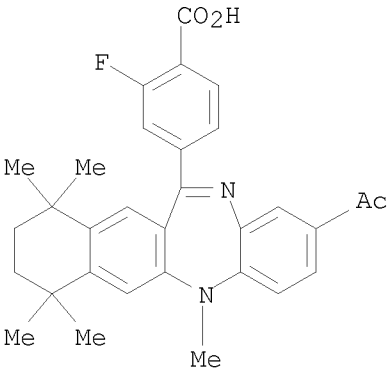
CN Benzoic acid, 4-(2-acetyl-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



RN 777074-36-9 CAPLUS
CN Benzoic acid, 4-(2-acetyl-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-3-fluoro- (CA INDEX NAME)

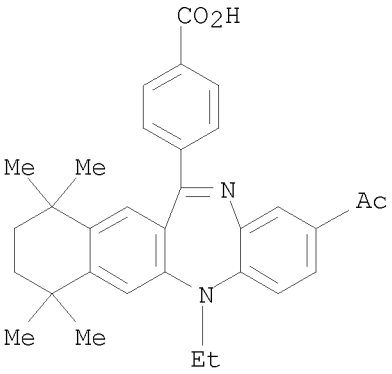


RN 777074-37-0 CAPLUS
CN Benzoic acid, 4-(2-acetyl-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-2-fluoro- (CA INDEX NAME)

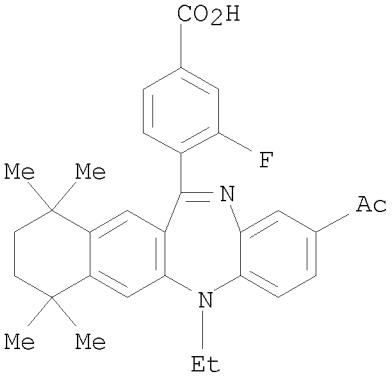


RN 777074-38-1 CAPLUS

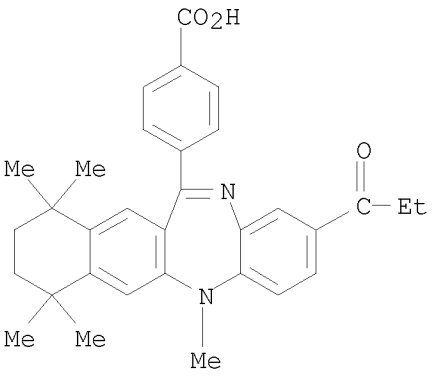
CN Benzoic acid, 4-(2-acetyl-5-ethyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



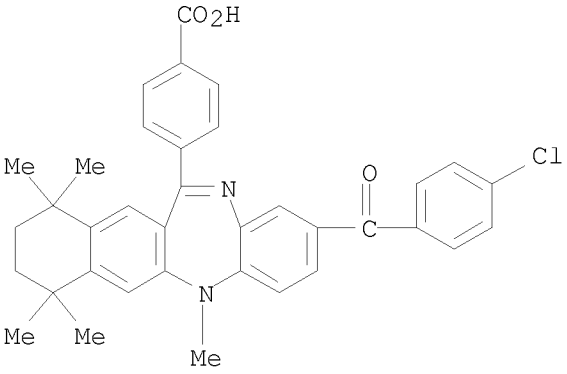
RN 777074-39-2 CAPLUS
CN Benzoic acid, 4-(2-acetyl-5-ethyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-3-fluoro- (CA INDEX NAME)



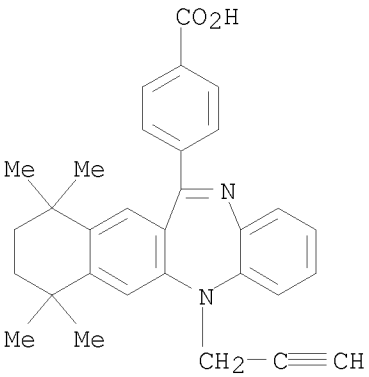
RN 777074-40-5 CAPLUS
CN Benzoic acid, 4-[7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-(1-oxopropyl)-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]- (CA INDEX NAME)



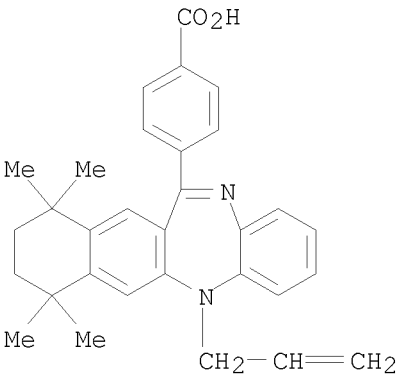
RN 777074-41-6 CAPLUS
CN Benzoic acid, 4-[2-(4-chlorobenzoyl)-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]- (CA INDEX NAME)



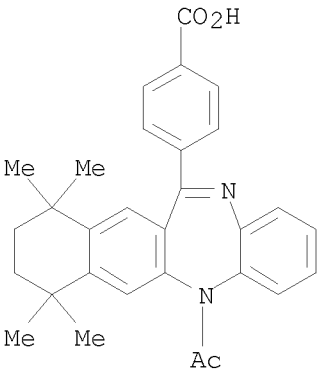
RN 777074-42-7 CAPLUS
CN Benzoic acid, 4-[7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-(2-propyn-1-yl)-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]- (CA INDEX NAME)



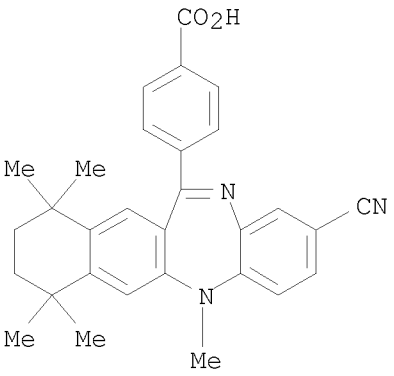
RN 777074-43-8 CAPLUS
CN Benzoic acid, 4-[7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-(2-propen-1-yl)-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]- (CA INDEX NAME)



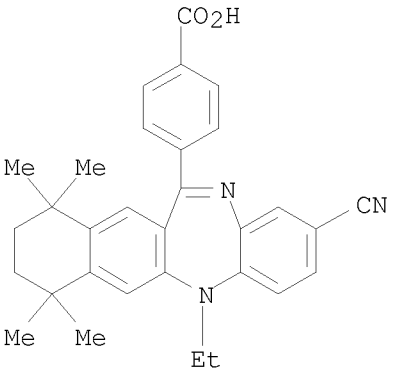
RN 777074-44-9 CAPLUS
CN Benzoic acid, 4-(5-acetyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



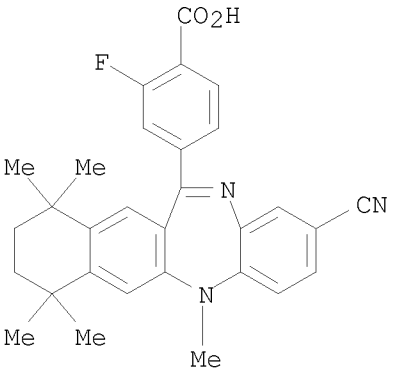
RN 777074-45-0 CAPLUS
CN Benzoic acid, 4-(2-cyano-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



RN 777074-46-1 CAPLUS
CN Benzoic acid, 4-(2-cyano-5-ethyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

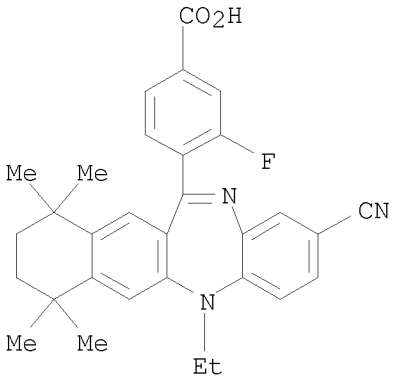


RN 777074-47-2 CAPLUS
CN Benzoic acid, 4-(2-cyano-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-2-fluoro- (CA INDEX NAME)

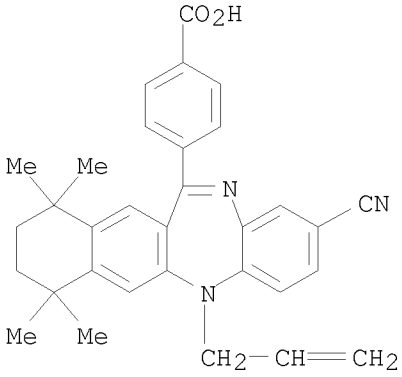


RN 777074-48-3 CAPLUS

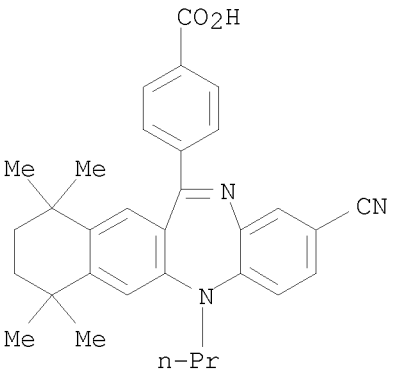
CN Benzoic acid, 4-(2-cyano-5-ethyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-3-fluoro- (CA INDEX NAME)



RN 777074-49-4 CAPLUS
CN Benzoic acid, 4-[2-cyano-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-(2-propen-1-yl)-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]- (CA INDEX NAME)

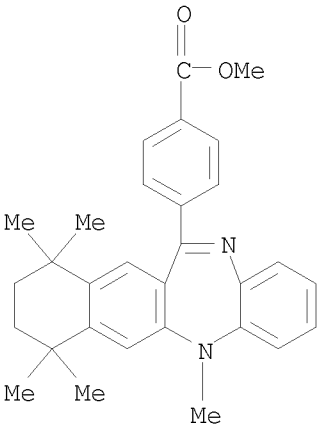


RN 777074-50-7 CAPLUS
CN Benzoic acid, 4-(2-cyano-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-propyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

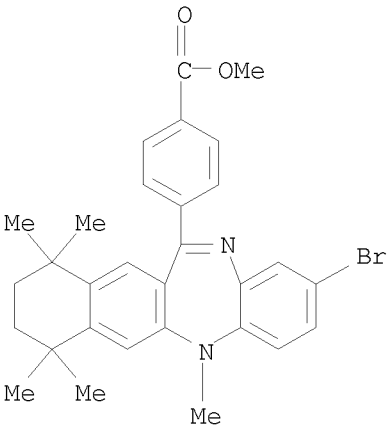


IT 188844-81-7P 259219-33-5P 777074-55-2P
777074-56-3P 777074-57-4P 777074-62-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 11-phenyldibenzodiazepine derivs. as RXR-antagonists for treatment of, e.g., diabetes)

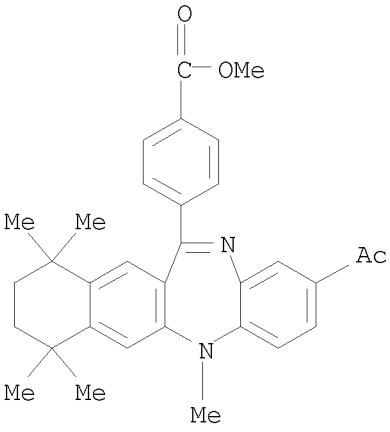
RN 188844-81-7 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



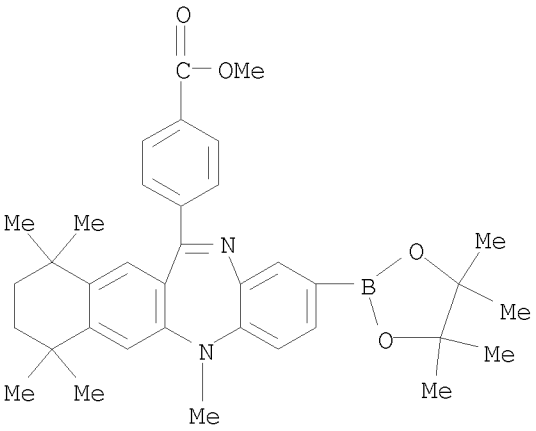
RN 259219-33-5 CAPLUS
CN Benzoic acid, 4-(2-bromo-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



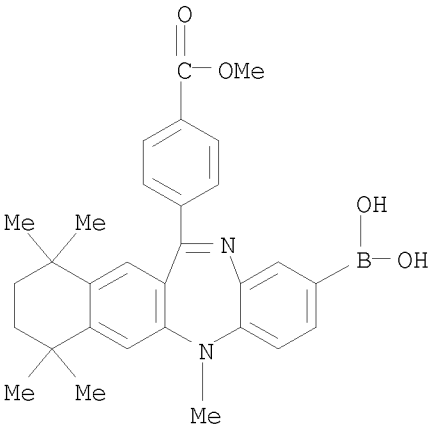
RN 777074-55-2 CAPLUS
CN Benzoic acid, 4-(2-acetyl-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



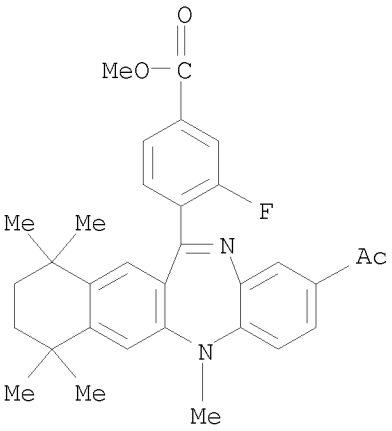
RN 777074-56-3 CAPLUS
CN Benzoic acid, 4-[7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]-, methyl ester (CA INDEX NAME)



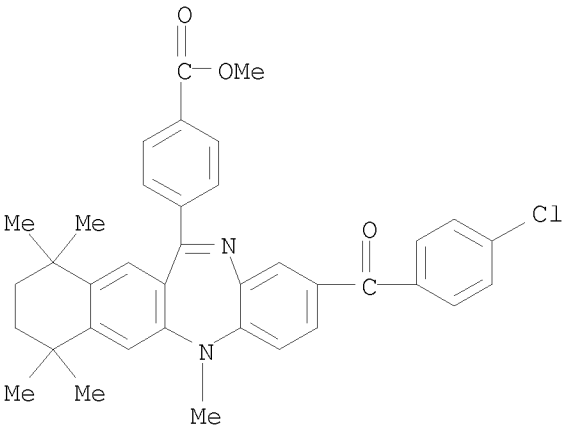
RN 777074-57-4 CAPLUS
CN Benzoic acid, 4-(2-borono-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, 1-methyl ester (9CI) (CA INDEX NAME)



RN 777074-62-1 CAPLUS
CN Benzoic acid, 4-(2-acetyl-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-3-fluoro-, methyl ester (CA INDEX NAME)



IT 888743-78-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 11-phenyldibenzodiazepine derivs. as RXR-antagonists for treatment of, e.g., diabetes)
RN 888743-78-0 CAPLUS
CN Benzoic acid, 4-[2-(4-chlorobenzoyl)-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]-, methyl ester (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:802847 CAPLUS
DOCUMENT NUMBER: 141:310214
TITLE: Organ-forming method
INVENTOR(S): Asashima, Makoto; Hamazaki, Tatsuo; Kagechika, Hiroyuki; Shudo, Koichi
PATENT ASSIGNEE(S): Research Foundation Itsuu Laboratory, Japan
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

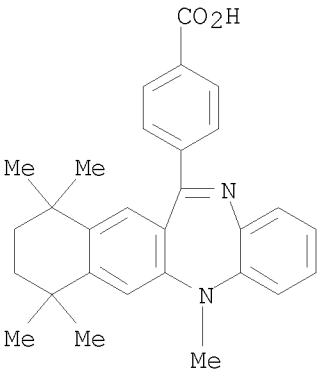
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004083413	A1	20040930	WO 2004-JP3578	20040317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004221524	A1	20040930	AU 2004-221524	20040317
CA 2523986	A1	20040930	CA 2004-2523986	20040317
EP 1612264	A1	20060104	EP 2004-721319	20040317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
US 20070161105	A1	20070712	US 2006-549816	20060901

PRIORITY APPLN. INFO.: JP 2003-77123 A 20030320
WO 2004-JP3578 W 20040317

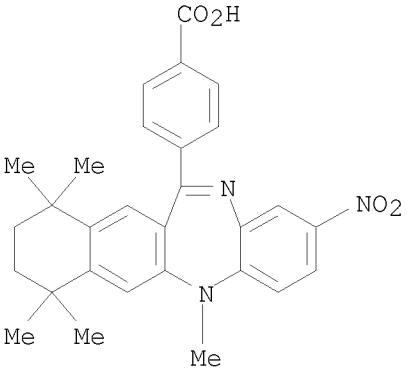
AB A method for forming an organ and/or tissue from undifferentiated vertebrate cells in vitro is provided, which involves a step for culturing undifferentiated vertebrate cells in the presence of a retinoic acid X receptor ligand (e.g., an agonist or an antagonist to retinoic acid X receptor). Also provided is a method for forming pancreas from undifferentiated vertebrate cells in vitro or a method for forming tissue having the form and functions of pancreas from undifferentiated vertebrate cells in vitro, which involves the step of culturing undifferentiated vertebrate cells in the presence of a retinoic acid X receptor ligand substantially not binding to retinoic acid receptor subtype γ, and activin.

IT 172705-89-4, HX 600 188844-34-0, HX531
259228-72-3, HX603
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(organ-forming method using cell differentiation agent)

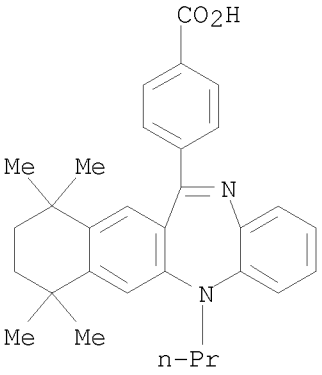
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

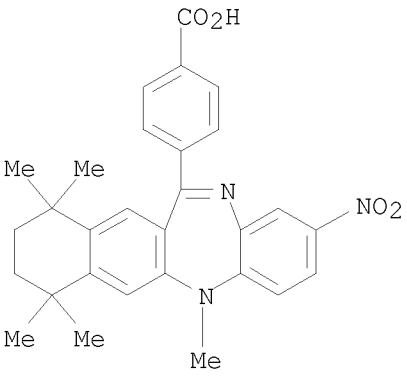


RN 259228-72-3 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-propyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:789514 CAPLUS
DOCUMENT NUMBER: 142:127342
TITLE: Docosahexaenoic acid reduces haloperidol-induced dyskinesias in mice: Involvement of Nur77 and retinoid receptors
AUTHOR(S): Ethier, Isabelle; Kagechika, Hiroyuki; Shudo, Koichi; Rouillard, Claude; Levesque, Daniel
CORPORATE SOURCE: CHUL Res. Cent., QC, Can.
SOURCE: Biological Psychiatry (2004), 56(7), 522-526
CODEN: BIPCBF; ISSN: 0006-3223
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Treatment of schizophrenia's symptoms with typical antipsychotic drugs shows some efficacy, but the induction of extrapyramidal symptoms represents a serious handicap, which considerably limits their usefulness. Recent evidence suggests that Nur77 (nerve growth factor-induced B) and retinoids are involved in biochem. and behavioral effects of antipsychotic drugs associated with striatal functions. Methods: We evaluated the effect of retinoid ligands on oral dyskinesias (vacuous chewing movements) induced by haloperidol in wild-type and Nur77-deficient mice. Results: Nur77 gene ablation (knockout) or administration of a retinoid antagonist induced vacuous chewing movements and exacerbated those induced by haloperidol, whereas the retinoid agonist docosahexaenoic acid (an ω-3 polyunsatd. fatty acid) reduced them. Both the prodyskinetic effect of the retinoid antagonist and the antidyskinetic effect of docosahexaenoic acid are dependent on the presence of Nur77, since these drugs remained inactive in Nur77 knockout mice. Conclusion: These results suggest that nuclear receptors Nur77 and retinoid X receptor are involved in haloperidol-induced dyskinesias and that retinoid agonists may represent a new way to improve typical antipsychotic drug therapy.
IT 188844-34-0, HX531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinoid X receptor agonist DHA showed antidyskinetic effect, reduced haloperidol-induced orofacial dyskinesias, retinoid antagonist HX-531 exacerbated orofacial dyskinesias in normal mouse and both drugs inactive in Nur 77 knockout mouse)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:756828 CAPLUS
DOCUMENT NUMBER: 141:274008
TITLE: Expansion of renewable stem cell populations using modulators of PI 3-kinase
INVENTOR(S): Peled, Tony; Grynspan, Frida
PATENT ASSIGNEE(S): Gamida-Cell Ltd., Israel
SOURCE: PCT Int. Appl., 249 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078917	A2	20040916	WO 2004-IL215	20040304
WO 2004078917	A3	20051027		
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WO 2003078567	A2	20030925	WO 2003-IL235	20030318
WO 2003078567	A3	20040610		
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WO 2004016731	A2	20040226	WO 2003-IL681	20030817
WO 2004016731	A3	20040910		
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AU 2004217699	A2	20040916	AU 2004-217699	20040304
AU 2004217699	A1	20040916		
AU 2004217699	B2	20080703		
CA 2517959	A1	20040916	CA 2004-2517959	20040304
EP 1601759	A2	20051207	EP 2004-717214	20040304
EP 1601759	A3	20051214		
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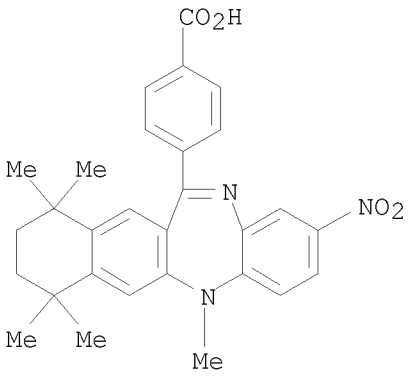
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK						
JP 2006521813	T	20060928	JP 2006-507579			20040304
AU 2005200679	A1	20050324	AU 2005-200679			20050216
ZA 2005007161	A	20060830	ZA 2005-7161			20050906
IN 2005CN02544	A	20070831	IN 2005-CN2544			20051005
PRIORITY APPLN. INFO.:			US 2003-452545P		P	20030307
			WO 2003-IL235		A	20030318
			WO 2003-IL681		A	20030817
			US 2002-364590P		P	20020318
			US 2002-404137P		P	20020819
			US 2002-404145P		P	20020819
			IL 2002-152904		A	20021117
			WO 2003-IL62		A	20030123
			WO 2003-IL64		A	20030126
			AU 2003-250519		A3	20030817
			WO 2004-IL215		W	20040304

AB Disclosed are ex vivo and in vivo methods of expansion of renewable stem cells using modulators of PI 3-kinase activity, expanded populations of renewable stem cells, and uses thereof. Treatment of enriched human CD34+ cell cultures with retinoic acid receptor antagonist AGN 194310 (prepared from 3-methyl-2-butenoic acid) and four human recombinant cytokines, thrombopoietin, interleukin 6, FLT-3 ligand and stem cell factor, resulted in large nos. of cells with a less differentiated phenotype in culture compared to cytokine only treated cell cultures. The RAR antagonist preferably enabled marked proliferation, yet limited differentiation of the stem cell compartment.

IT 188844-34-0P, HX 531
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(as RAR+RXR antagonist for hematopoietic cell expansion; ex vivo and in vivo expansion of renewable stem cell populations using modulators of PI 3-kinase and uses in transduction, transplantation and therapy)

RN 188844-34-0 CAPLUS

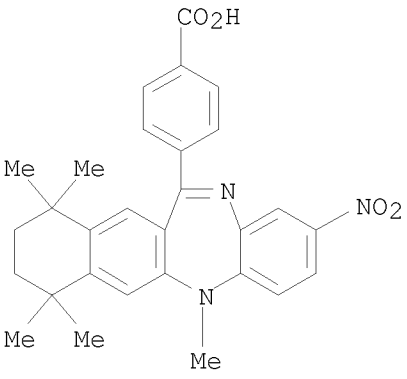
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



L25 ANSWER 18 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:749997 CAPLUS
DOCUMENT NUMBER: 139:255334
TITLE: Compositions and methods using an RXR agonist and a protein kinase A activator for the treatment of hyperproliferative diseases
INVENTOR(S): Benoit, Gerard; Gronemeyer, Hinrich; Lanotte, Michel; Gottardis, Marco
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Institut National de la Sante et de la Recherche Medicale; Centre National de la Recherche Scientifique; Universite Louis Pasteur
SOURCE: U.S., 35 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6624154	B1	20030923	US 2000-556675		20000421
PRIORITY APPLN. INFO.:			US 1999-130649P	P	19990423

OTHER SOURCE(S): MARPAT 139:255334
AB The invention discloses compns. comprising a retinoid X receptor agonist and an agent capable of activating protein kinase A. The invention also discloses methods for treating hyperproliferative diseases (e.g. leukemia, breast cancer) by administering a retinoid X receptor agonist and an agent capable of activating protein kinase A. Prepn of 4-[1-(5,6-dihydro-3,5,5-trimethyl-8-isopropyl-2-naphthalenyl)ethenyl] benzoic acid is described.
IT 188844-34-0, HX531
RL: PAC (Pharmacological activity); BIOL (Biological study)
(RXR agonist and protein kinase A activator for treatment of hyperproliferative diseases, and use with other agents)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L25 ANSWER 19 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:591288 CAPLUS
DOCUMENT NUMBER: 139:148489
TITLE: Cytokines and retinoic acid receptor antagonists for expansion of renewable stem cells and adoptive immunotherapy
INVENTOR(S): Peled, Tony; Treves, Avi; Rosen, Oren
PATENT ASSIGNEE(S): Gamida-Cell Ltd., Israel
SOURCE: PCT Int. Appl., 316 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062369	A2	20030731	WO 2003-IL64	20030126
WO 2003062369	A3	20060330		
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CA 2474344	A1	20030731	CA 2003-2474344	20030126
EP 1576089	A2	20050921	EP 2003-706871	20030126
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JP 2005528088	T	20050922	JP 2003-562237	20030126
AU 2003208577	B2	20080710	AU 2003-208577	20030126
AU 2003208577	B9	20080731		
CA 2479679	A1	20030925	CA 2003-2479679	20030318
WO 2003078567	A2	20030925	WO 2003-IL235	20030318
WO 2003078567	A3	20040610		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2003214614	A1	20030929	AU 2003-214614	20030318
EP 1485464	A2	20041215	EP 2003-710194	20030318
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JP 2005520511	T	20050714	JP 2003-576562	20030318
CA 2495824	A1	20040226	CA 2003-2495824	20030817
WO 2004016731	A2	20040226	WO 2003-IL681	20030817
WO 2004016731	A3	20040910		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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AU 2003250519	A1	20040303	AU 2003-250519		20030817
EP 1534820	A2	20050601	EP 2003-787995		20030817
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BR 2003014402	A	20050719	BR 2003-14402		20030817
JP 2006508692	T	20060316	JP 2005-502022		20030817
US 20050008624	A1	20050113	US 2004-774843		20040209
ZA 2004005901	A	20060426	ZA 2004-5901		20040723
AU 2005200679	A1	20050324	AU 2005-200679		20050216
MX 2005PA01992	A	20050803	MX 2005-PA1992		20050218
ZA 2005002111	A	20050914	ZA 2005-2111		20050314
US 20050220774	A1	20051006	US 2005-508244		20050519
PRIORITY APPLN. INFO.:			US 2002-350360P	P	20020124
			US 2002-376183P	P	20020430
			US 2002-404137P	P	20020819
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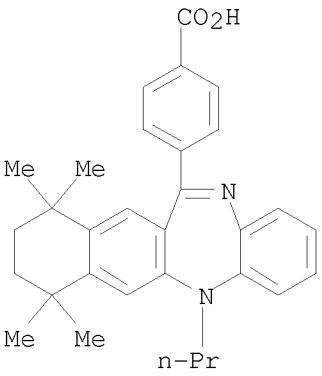
			US 2003-452545P	P	20030307
			WO 2003-IL235	W	20030318
			AU 2003-250519	A3	20030817
			WO 2003-IL681	W	20030817

AB Disclosed are methods for ex vivo and in vivo expansion of renewable stem cells for transplantation or implantation. The stem cell expansion is achieved by stimulating proliferation and inhibiting differentiation of hematopoietic stem cells. The proliferation of stem cells is stimulated by cytokine such as stem cell factor, FLT3 ligand, interleukin 6, interleukin 1, interleukin 2, interleukin 10, interleukin 12, tumor necrosis factor α, thrombopoietin, interleukin 3, G-CSF, M-CSF, GM-CSF and erythropoietin, FGF, EGF, NGF, VEGF, LIF, and hepatocyte growth factor. The expression of CD38 and differentiation of stem cells is inhibited by antibodies or antagonists of retinoic acid receptor, retinoid X receptor, and vitamin D receptor.

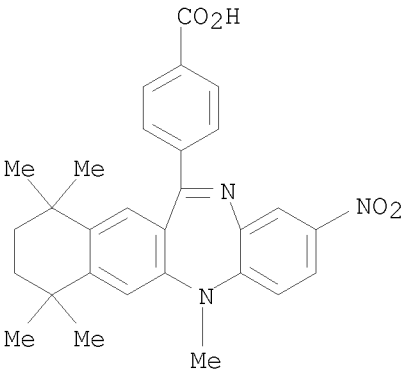
IT 259228-72-3
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cytokines and retinoic acid receptor antagonists for expansion of renewable stem cells and adoptive immunotherapy)

RN 259228-72-3 CAPLUS

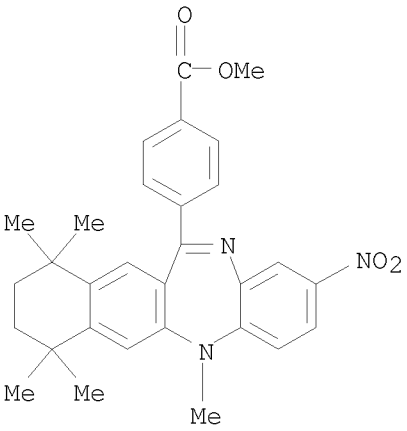
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-propyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



IT 188844-34-0P, HX 531
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cytokines and retinoic acid receptor antagonists for expansion of renewable stem cells and adoptive immunotherapy)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



IT 188845-12-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cytokines and retinoic acid receptor antagonists for expansion of renewable stem cells and adoptive immunotherapy)
RN 188845-12-7 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)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L25 ANSWER 20 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:335065 CAPLUS
DOCUMENT NUMBER: 138:368620
TITLE: Preparation of 2-chloro-5-nitrobenzamides as lipid modulators for treatment of osteoporosis and diabetes
INVENTOR(S): Amemiya, Yoshiya; Wakabayashi, Kenji; Takaishi, Sachiko; Kitayama, Ken
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035602	A1	20030501	WO 2002-JP11068	20021024
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2002338204	A1	20030506	AU 2002-338204	20021024
JP 2003201271	A	20030718	JP 2002-310549	20021025
PRIORITY APPLN. INFO.:			JP 2001-327189 A	20011025
			WO 2002-JP11068 W	20021024

OTHER SOURCE(S): MARPAT 138:368620
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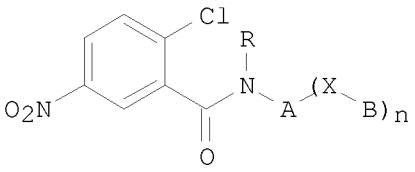


I

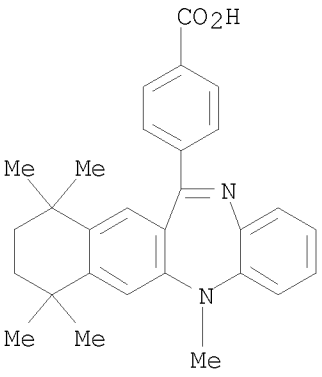
AB The title compds. I [wherein A = (un)substituted Ph, naphthyl, acenaphthenyl, Py, (iso)quinolyl, pyrimidyl, (benzo)furyl, pyranyl, chromanyl, (benzo)thienyl, pyrrolyl, (iso)indolyl, imidazolyl, pyrazolyl, pyridazinyl, pyrazinyl, (iso)oxazolyl, pyrrolidinyl, piperidyl, piperazyl, benzoxazolyl, benzoisooxazolyl, (iso)thiazolyl, benzothiazolyl, or biphenyl; B = (un)substituted aryl, cycloalkyl, or heterocyclyl; R = H or alkyl; X = a bond, O, S, CH2, CO, NH, SO2NH, NHSO2, CONH, NHCO, or OCH2; n = 0-1] and pharmaceutically acceptable salts thereof are prepared as lipid modulators for treatment of osteoporosis and diabetes. For example, 4-phenylaniline hydrochloride was reacted with 2-chloro-5-nitrobenzoyl

chloride in pyridine to afford N-(4-phenylphenyl)-2-chloro-5-nitrobenzamide. The above N-(4-phenylphenyl)-2-chloro-5-nitrobenzamide showed IC50 of 1.9 nM against human PPAR γ. I are useful for the treatment of osteoporosis, and diabetes, etc.

IT 172705-89-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chloro(nitro)benzamides as lipid modulators for treatment of osteoporosis and diabetes)

RN 172705-89-4 CAPLUS

CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



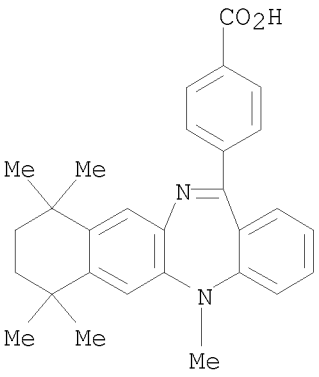
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:259124 CAPLUS
DOCUMENT NUMBER: 139:4424
TITLE: Regulation of cardiovascular remodeling by transcription factor KLF5/BTEB2
AUTHOR(S): Shindo, Takayuki; Manabe, Ichiro; Nagai, Ryozo
CORPORATE SOURCE: School of medicine, Dep. of Circulatory Diseases, University of Tokyo, Japan
SOURCE: Ketsuatsu (2003), 10(3), 242-245
CODEN: KETSAH; ISSN: 1340-4598
PUBLISHER: Sentan Igakusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on Krueppel-like transcription factor 5 (KLF5)/basic transcription element binding protein-2 (BTEB2) in regulating angiotensin II signaling and cardiovascular remodeling. The topics discussed are (1) diminished arterial-wall thickening, angiogenesis, cardiac hypertrophy and interstitial fibrosis in heterozygous KLF5/BTEB2 knockout mice; (2) KLF5/BTEB2 in regulating transcriptional activation of the platelet-derived growth factor-A (PDGF-A); and (3) synthetic retinoic-acid receptor (RAR) ligands Am 80 and LE 135 in modulating KLF5/BTEB2 transcriptional activity and their roles in therapy.

IT 155877-83-1, LE 135
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transcription factor KLF5/BTEB2 in regulating angiotensin II signaling and cardiovascular remodeling and role of)

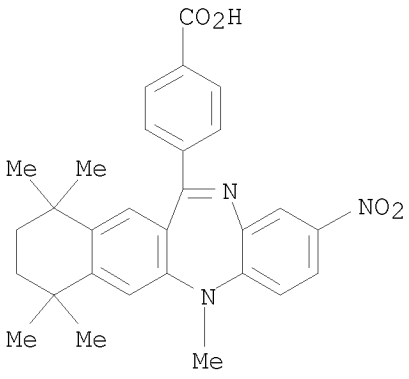
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



L25 ANSWER 22 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:32697 CAPLUS
DOCUMENT NUMBER: 138:182789
TITLE: Effects of Retinoid Ligands on RIP140: Molecular Interaction with Retinoid Receptors and Biological Activity
AUTHOR(S): Farooqui, Mariya; Franco, Peter J.; Thompson, Jim; Kagechika, Hiroyuki; Chandraratna, Roshantha A. S.; Banaszak, Len; Wei, Li-Na
CORPORATE SOURCE: Departments of Pharmacology and Biochemistry, University of Minnesota Medical School, Minneapolis, MN, 55455, USA
SOURCE: Biochemistry (2003), 42(4), 971-979
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Receptor interacting protein 140 (RIP140) interacts with retinoic acid receptor (RAR) and retinoid X receptor (RXR) constitutively, but hormone binding enhances this interaction. The ligand-independent interaction is mediated by the amino and central regions of RIP140 which contain a total of nine copies of the LXXLL motif, whereas the agonist-induced interaction is mediated by its carboxyl terminus which contains a novel motif (1063-1076, LTKTNPILYYMLQK). The ligand-independent interaction could be enhanced slightly by agonists, whereas the ligand-dependent interaction was strictly agonist dependent for both RAR and RXR. In the context of heterodimers, ligand occupancy of RXR played a more dominant role for both mol. interaction and biol. activity of RIP140. Competition and mutation studies demonstrated an essential role for 1067Asn and 1073Met for a ligand-dependent interaction. A model was proposed to address the constitutive and agonist-dependent interaction of RIP140 with RAR/RXR.

IT 188844-34-0, HX531
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand; effects of retinoid ligands on receptor interacting protein RIP140 mol. interaction with retinoid receptors and biol. activity)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



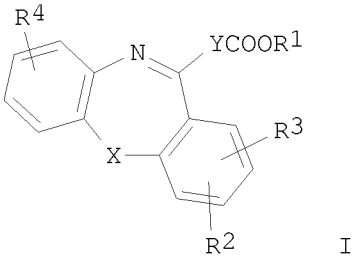
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:945583 CAPLUS
DOCUMENT NUMBER: 137:380030
TITLE: Benzodiazepine derivatives as preventives/remedies for diabetes
INVENTOR(S): Kagechika, Hiroyuki; Hashimoto, Yuichi; Fujii, Hideji; Yonekawa, Yoshiaki; Ekimoto, Hisao
PATENT ASSIGNEE(S): Institute of Medicinal Molecular Design Inc., Japan
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

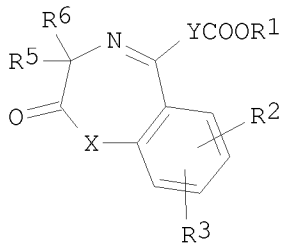
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6458782	B1	20021001	US 2000-555508	20000901
JP 11171776	A	19990629	JP 1997-335956	19971205
WO 9929324	A1	19990617	WO 1998-JP5480	19981204

W: AU, CA, CN, ID, KR, NO, SG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: JP 1997-335956 A 19971205
WO 1998-JP5480 W 19981204
OTHER SOURCE(S): MARPAT 137:380030
GI



I

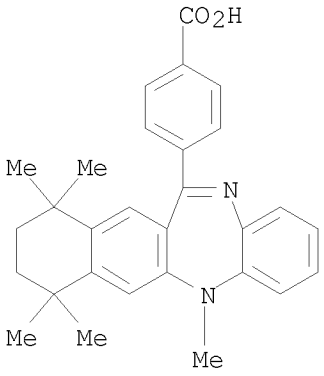


II

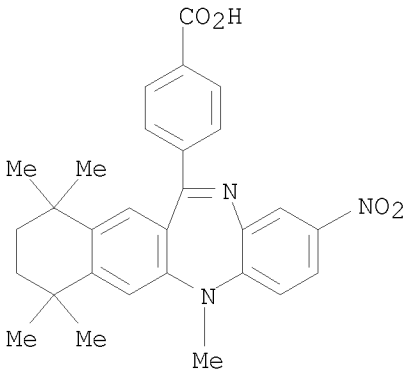
AB Benzodiazepine derivs. containing as the active ingredient compds. represented by general formula (I and II) and being useful in preventing and treating diabetes and complication thereof, wherein R1 represents hydrogen or C1-6 alkyl; R2 and R3 represent each hydrogen or C1-6 alkyl, or R2 and R3 may form together with the carbon atom on the Ph ring to which they are bonded a 5- or 6-membered ring; R4 represents hydrogen, C1-6 alkyl, C1-6 alkoxy, etc.; R6 represents hydrogen or C1-6 alkyl; X represents -NR7-, -NO-, -O-, etc. (wherein R7 represents hydrogen, C1-6 alkyl, etc.); and Y represents phenylene or pyridinediyl. I and II are claimed as oral antidiabetics and hypolipidemics and have synergistic effect with other antidiabetics.
IT 172705-89-4, HX600 188844-34-0, HX 531
203920-36-9, HX 610 203920-47-2, HX 511
227328-77-0, Benzoic acid, 4-(2,11-dihydro-11-methyl-1H-benzo[e]cyclobuta[3,4]benzo[1,2-b][1,4]diazepin-6-yl)-
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(benzodiazepine derivs. as preventives/remedies for diabetes)

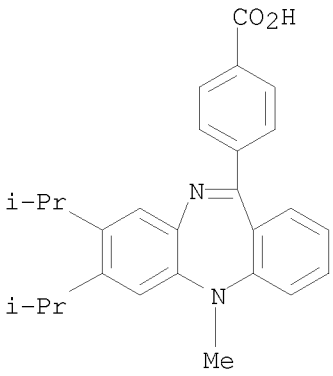
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



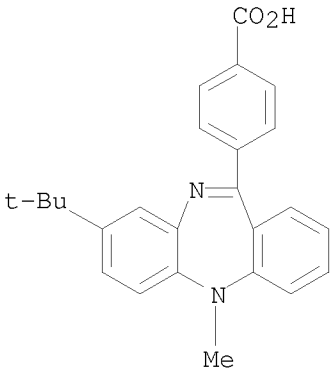
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



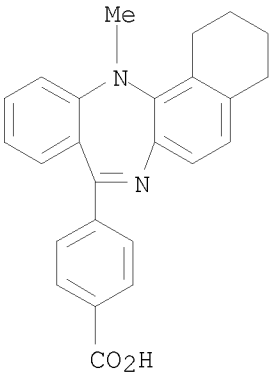
RN 203920-36-9 CAPLUS
CN Benzoic acid, 4-[5-methyl-7,8-bis(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



RN 203920-47-2 CAPLUS
CN Benzoic acid, 4-[8-(1,1-dimethylethyl)-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



RN 227328-77-0 CAPLUS
CN Benzoic acid, 4-(2,3,4,13-tetrahydro-13-methyl-1H-benzo[e]naphtho[2,1-b][1,4]diazepin-8-yl)- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 24 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:907167 CAPLUS
DOCUMENT NUMBER: 138:16588
TITLE: Method for modulating expression of exogenous genes in mammalian systems using modified ecdysone receptors for gene therapy
INVENTOR(S): Evans, Ronald M.; No, David; Saez, Enrique
PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA
SOURCE: U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S. Ser. No. 974,530, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

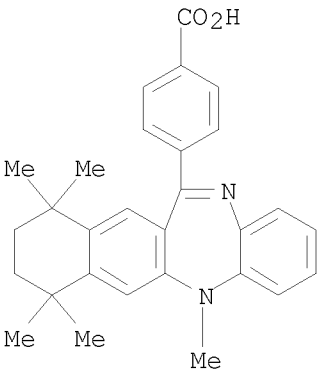
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020177564	A1	20021128	US 1998-42488	19980316
US 6723531	B2	20040420		
US 20060014711	A1	20060119	US 2004-828831	20040420

PRIORITY APPLN. INFO.: US 1996-628830 B2 19960405
US 1997-974530 B2 19971119
US 1998-42488 A1 19980316

AB The present invention provides various methods for modulating the expression of an exogenous gene in a mammalian subject employing modified ecdysone (ecdysteroid) receptors in steroid inducible system. Modified ecdysone receptors can be in the form of homodimeric species or heterodimeric species comprising at least one silent partner of the steroid/thyroid hormone superfamily of receptors, along with an invention modified ecdysone receptor. There are provided nucleic acids encoding modified ecdysone receptors, modified ecdysone receptor response elements, gene transfer vectors, recombinant cells, and transgenic animals containing nucleic acid encoding invention modified ecdysone receptor. The invention method is useful in a wide variety of applications where inducible in vivo expression of an exogenous gene is desired, such as in vivo therapeutic methods for delivering recombinant proteins into a variety of cells within a patient.

IT 172705-89-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for modulating expression of exogenous genes in mammalian systems using modified ecdysone receptors for gene therapy)

RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 118 THERE ARE 118 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 25 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:658237 CAPLUS
DOCUMENT NUMBER: 137:196635
TITLE: Novel substitution variants of nuclear receptors and their use in a dual switch inducible system for regulation of gene expression
INVENTOR(S): Palli, Subba Reddy; Kapitskaya, Marianna Zinovjevna
PATENT ASSIGNEE(S): Rohm and Haas Company, USA; Rheogene Inc.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066615	A2	20020829	WO 2002-US5708	20020220
WO 2002066615	A9	20040129		
WO 2002066615	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2438133	A1	20020829	CA 2002-2438133	20020220
AU 2002248500	A1	20020904	AU 2002-248500	20020220
AU 2002248500	B2	20071213		
JP 2004533216	T	20041104	JP 2002-566322	20020220
EP 1534738	A2	20050601	EP 2002-717504	20020220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
MX 2003PA07494	A	20041015	MX 2003-PA7494	20030820
AU 2007200882	A1	20070322	AU 2007-200882	20070228

PRIORITY APPLN. INFO.:	US 2001-269799P	P	20010220
	US 2001-313908P	P	20010821
	WO 2002-US5708	W	20020220

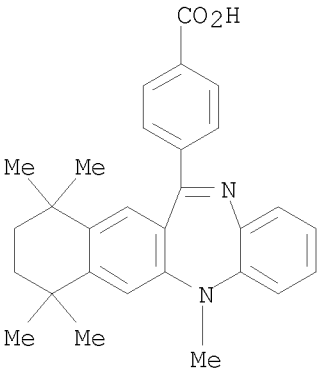
OTHER SOURCE(S): MARPAT 137:196635
AB Novel substitution mutant of nuclear receptors, specifically Group H nuclear receptors, that show improved ligand responsiveness that can be used to modulate gene expression in a host cell for applications such as gene therapy, large scale production of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic organisms. In particular, one gene expression cassette is inducibly regulated by a steroid ligand and the other gene expression cassette is inducibly regulated by a non-steroid ligand. Specific embodiments of the invention provide ecdysone receptor ligand-binding domains fused to the DNA-binding domains of GAL4 or LexA, and the ligand-binding domains of retinoid X receptor or ultraspiracle protein fused to the VP16 transactivation domain. A series of substitution mutants of insect ecdysteroid receptors were prepared by standard PCR mutagenesis and tested for their responsiveness to ecdysteroid

induction of reporter gene expression in the dual switch system. Variants that showed increased responsiveness to the ecdysteroids with decreased responsiveness to non-steroid ligands were identified. Variants showed increased responsiveness to both classes of effectors, or to nonsteroids but not ecdysteroids, were also identified.

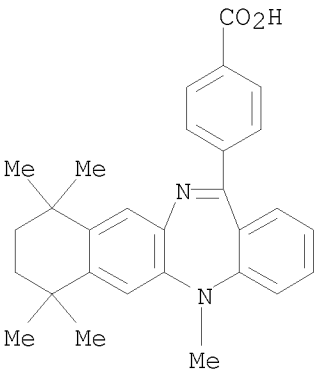
IT 172705-89-4D, HX600, thiadiazepine analogs
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulation of receptor function and gene expression by; novel substitution variants of nuclear receptors and their use in dual switch inducible system for regulation of gene expression)

RN 172705-89-4 CAPLUS

CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



L25 ANSWER 26 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:569540 CAPLUS
DOCUMENT NUMBER: 137:320646
TITLE: Krueppel-like zinc-finger transcription factor KLF5/BTEB2 is a target for angiotensin II signaling and an essential regulator of cardiovascular remodeling
AUTHOR(S): Shindo, Takayuki; Manabe, Ichiro; Fukushima, Yasushi; Tobe, Kazuyuki; Aizawa, Kenichi; Miyamoto, Saku; Kawai-Kowase, Keiko; Moriyama, Nobuo; Imai, Yasushi; Kawakami, Hayato; Nishimatsu, Hiroaki; Ishikawa, Takashi; Suzuki, Toru; Morita, Hiroyuki; Maemura, Koji; Sata, Masataka; Hirata, Yasunobu; Komukai, Masayuki; Kagechika, Hiroyuki; Kadowaki, Takashi; Kurabayashi, Masahiko; Nagai, Ryozo
CORPORATE SOURCE: Department of Cardiovascular Medicine, University of Tokyo, Tokyo, Japan
SOURCE: Nature Medicine (New York, NY, United States) (2002), 8(8), 856-863
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We recently isolated a Krueppel-like zinc-finger transcription factor 5 (KLF5; also known as BTEB2 and IKLF), which is markedly induced in activated vascular smooth-muscle cells and fibroblasts. Here we describe our anal. of the in vivo function of KLF5 using heterozygous KLF5-knockout mice (Klf5+/-). In response to external stress, Klf5+/- mice showed diminished levels of arterial-wall thickening, angiogenesis, cardiac hypertrophy and interstitial fibrosis. Also, angiotensin II induced expression of KLF5, which in turn activated platelet-derived growth factor-A (PDGF-A) and transforming growth factor-β (TGF-β) expression. In addition, we determined that KLF5 interacted with the retinoic-acid receptor (RAR), that synthetic RAR ligands modulated KLF5 transcriptional activity, and that in vivo administration of RAR ligands affected stress responses in the cardiovascular system in a KLF5-dependent manner. KLF5 thus seems to be a key element linking external stress and cardiovascular remodeling.
IT 155877-83-1, LE 135
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transcription factor KLF5 as target for angiotensin II signaling and an essential regulator of cardiovascular remodeling and retinoids regulation thereof)
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)

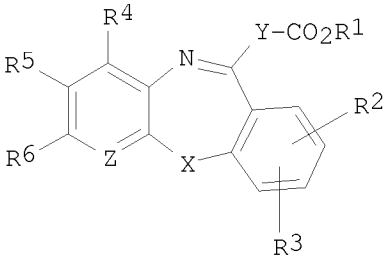


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

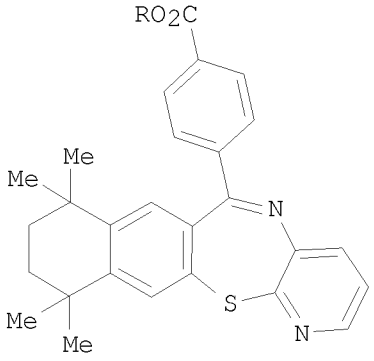
L25 ANSWER 27 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:539685 CAPLUS
DOCUMENT NUMBER: 137:93779
TITLE: Preparation of naphtho[2,3-f]pyrido[2,3-b][1,4]thiazepine and benzo[b]naphtho[2,3-f][1,4]thiazepine derivatives as retinoid agonists
INVENTOR(S): Nagano, Tatsuo; Saotome, Tomomi; Itai, Akiko
PATENT ASSIGNEE(S): Institute of Medicinal Molecular Design Inc., Japan
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055525	A1	20020718	WO 2002-JP81	20020110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002219580	A1	20020724	AU 2002-219580	20020110
JP 4121853	B2	20080723	JP 2002-556194	20020110
PRIORITY APPLN. INFO.:			JP 2001-4992 A	20010112
			WO 2002-JP81 W	20020110

OTHER SOURCE(S): MARPAT 137:93779
GI



I



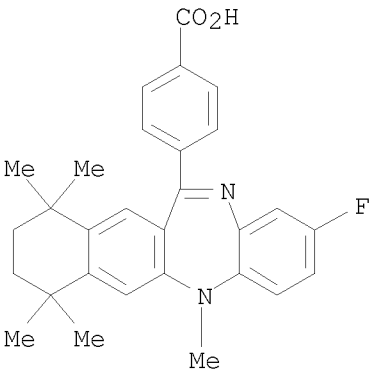
II

AB Compds. represented by the general formula (I) or salts thereof [wherein R1 = H, C1-6 alkyl; R2, R3 = H, C1-6 alkyl; or R2 and R3 together with the carbon atoms on the benzene ring to which they are bonded form a 5- or

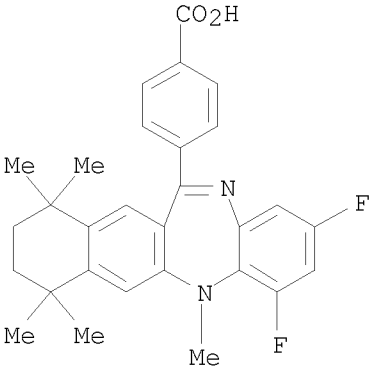
6-membered ring; R4, R5, R6 = H, halo, C1-6 alkyl, C1-6 haloalkyl; Y = phenylene, pyridinediyl; X = S or N(R7) (wherein R7 = H, C1-6 alkyl); Z = CR8 (wherein R8 = H, halogeno, C1-6 alkyl, C1-6 haloalkyl) or N] are prepared These compds. have an ability to potentiate the physiol. activities of nuclear receptor ligands such as retinoic acid or retinoids and are useful for the prevention and/or treatment of vitamin A deficiency, keratosis of epithelial tissue, psoriasis, allergies, immune diseases such as rheumatism, bone diseases, leukemia, diabetes, and cancer. They also potentiate the physiol activities of steroids, vitamin D compds. such as vitamin D3, and thyroxine which manifest the physiol. activities by binding to receptors belonging to inner receptor super-family present in cell nucleus. Thus, treatment of 5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalene-2-thiol with NaH in DMF at room temperature for 1 h followed thioetherification with 2-chloro-3-nitropyridine at room temperature for 2 h gave 3-nitro-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalen-2-ylthio)pyridine which underwent reduction with Fe/HCl in aqueous ethanol to 3-amino-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalen-2-ylthio)pyridine followed by amidation with 4-methoxycarbonylbenzoyl chloride in the presence of Et3N in CH2Cl2 to give N-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalen-2-ylthio)pyridin-3-yl]-4-methoxycarbonylbenzamide (II). Cyclization of II in polyphosphoric acid at 120° for 1 h gave naphtho[2,3-f]pyrido[2,3-b][1,4]thiazepine derivative (III; R = Me) which was hydrolyzed by a mixture of 2 N aqueous NaOH, THF, and MeOH and acidified with 2 N aqueous HCl to give III (R = H). Although III (R = H) showed the induction of cell differentiation in human leukemia HL-60 cells by 0.8, 0.8, and 0.4% at 10-8, 10-7, and 10-6 M, resp., when tested alone, but it showed the cell differentiation induction ratio of 24, 23, 45, and 88% at 10-10, 10-9, 10-8, and 10-7 M, resp., in the presence of 10-10 M Am80, i.e. 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid, vs. 13.5% when Am80 was tested alone at 10-10 M.

IT 442691-44-3P 442691-45-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naphtho[f]pyrido[b][1,4]thiazepine and benzo[b]naphtho[f][1,4]thiazepine derivs. as retinoid agonists for prevention and/treatment of diseases)

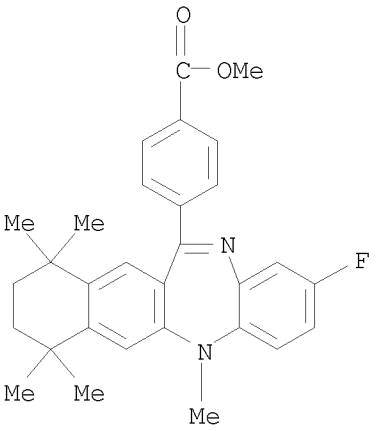
RN 442691-44-3 CAPLUS
CN Benzoic acid, 4-(2-fluoro-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



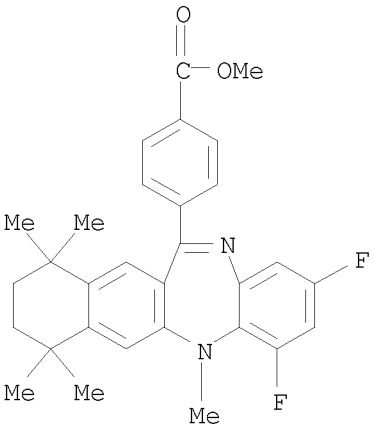
RN 442691-45-4 CAPLUS
CN Benzoic acid, 4-(2,4-difluoro-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



IT 442691-42-1P 442691-43-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of naphtho[f]pyrido[b][1,4]thiazepine and benzo[b]naphtho[f][1,4]thiazepine derivs. as retinoid agonists for prevention and/treatment of diseases)
RN 442691-42-1 CAPLUS
CN Benzoic acid, 4-(2-fluoro-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



RN 442691-43-2 CAPLUS
CN Benzoic acid, 4-(2,4-difluoro-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)

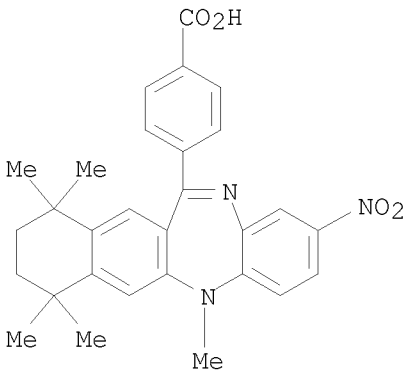


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 28 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:515545 CAPLUS
DOCUMENT NUMBER: 137:210746
TITLE: Novel Retinoid X Receptor Antagonists: Specific Inhibition of Retinoid Synergism in RXR-RAR Heterodimer Actions
AUTHOR(S): Takahashi, Bitoku; Ohta, Kiminori; Kawachi, Emiko; Fukasawa, Hiroshi; Hashimoto, Yuichi; Kagechika, Hiroyuki
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, The University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: Journal of Medicinal Chemistry (2002), 45(16), 3327-3330
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several 2-(arylamino)pyrimidine-5-carboxylic acids were designed as novel retinoid X receptor (RXR) antagonists. Two of the tested compds. alone did not exhibit differentiation-inducing activity toward HL-60 cells and did not affect the activity of a retinoic acid receptor (RAR) agonist, Am80, but did inhibit the synergistic activity of an RXR agonist, PA024, in the presence of Am80. The activity of these compds. was ascribed to selective antagonism at the RXR site of RXR-RAR heterodimers.

IT 188844-34-0, HX 531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HX 531; preparation and activity of retinoid X receptor antagonists)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



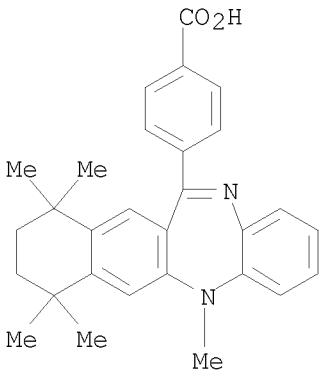
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 29 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:198164 CAPLUS
DOCUMENT NUMBER: 136:257594
TITLE: Thyroid hormone affects retinoid-induced cellular differentiation in promyeloleukemic HL-60 cells
AUTHOR(S): Hara, Masahiro; Suzuki, Satoru
CORPORATE SOURCE: Dep. Aging Med. Geriatr., Shinshu Univ. Sch. Med., Japan
SOURCE: Horumon to Rinsho (2002), 50(2), 223-232
CODEN: HORIAE; ISSN: 0045-7167
PUBLISHER: Igaku no Sekaisha
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB All-trans retinoic acid (ATRA) induces apoptosis in HL60 cells, which is enhanced by thyroid hormone. The enhancement was by different mechanism between retinoid acid receptor (RAR) ligand and retinoid X receptor (RXR) receptor ligand. Am80 and HX600 4-[5H-2,3-(2,5-dimethyl-2,5-hexano)-5-methyldibenzo[b,e][1,4]diazepin-11-yl]benzoic acid were used for an RAR-specific ligand and an RXR-specific ligand, resp. 3,5,3'-Triiodo-L-thyronine (T3) was used for thyroid hormone. Am80 suppressed proliferation of HL-60 in the presence of 0.1% ethanol, and the degree of suppression reached to the level similar to ATRA when Am80 + HX600 was used (Am80 and HX600 were at 10-6M). The proliferation was suppressed by dose-dependent manner by T3, T3 + ATRA. T3 + Am80 and T3 + HX600. T3 + Am80 induced apoptosis and cell differentiation, whereas T3 + HX600 induced apoptosis alone. T3 + Am80 increased population of G0/G1 phase, showing RAR participated in the regulation of cell cycle. T3 + Am80 increased surface expression of CD11b. T3 + ATRA increased expression of bfl1 and bcl2, which also occurred by T3 + Am80.

IT 172705-89-4, HX 600
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thyroid hormone affects retinoid-induced cellular differentiation in HL-60 cells)

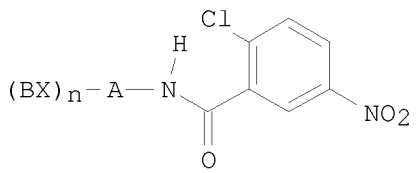
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



L25 ANSWER 30 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:816614 CAPLUS
DOCUMENT NUMBER: 135:357944
TITLE: Preparation of nitrophenylcarboxamide derivatives as peroxisome proliferator-activated receptor (PPAR) γ modulators
INVENTOR(S): Amemiya, Yoshiya; Wakabayashi, Kenji; Takaishi, Sachiko; Fukuda, Chie
PATENT ASSIGNEE(S): Sankyo Company, Ltd., Japan
SOURCE: PCT Int. Appl., 186 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001083427	A1	20011108	WO 2001-JP3655		20010426
W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU, US, ZA					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
CA 2407587	A1	20011108	CA 2001-2407587		20010426
AU 2001052612	A	20011112	AU 2001-52612		20010426
EP 1277729	A1	20030122	EP 2001-925984		20010426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR					
BR 2001010428	A	20030617	BR 2001-10428		20010426
HU 2003001146	A2	20030828	HU 2003-1146		20010426
HU 2003001146	A3	20040830			
JP 2002332266	A	20021122	JP 2001-130983		20010427
ZA 2002008465	A	20040212	ZA 2002-8465		20021018
IN 2002KN01314	A	20040501	IN 2002-KN1314		20021022
US 20030134859	A1	20030717	US 2002-278387		20021023
NO 2002005142	A	20021227	NO 2002-5142		20021025
MX 2002PA10651	A	20030310	MX 2002-PA10651		20021028
PRIORITY APPLN. INFO.:			JP 2000-129565	A	20000428
			JP 2001-60366	A	20010305
			WO 2001-JP3655	W	20010426

OTHER SOURCE(S): MARPAT 135:357944
GI



I

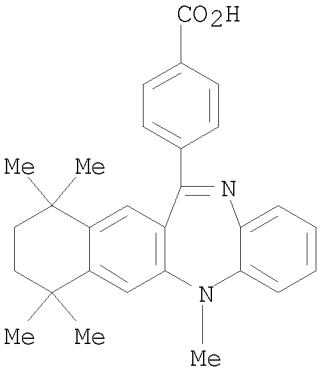
AB The title compds. I [A represents Ph, etc.; B represents aryl, etc.; X represents oxygen, etc.; and n is 0 or 1] are prepared I are remedies for involutional osteoporosis which inhibit the accelerated differentiation of adipocytes and promote the formation and differentiation of osteoblasts from stem cells; I are also remedies for diabetes. In an in vitro test

for PPAR γ modulating activity, N-[4-(4-methylpiperazin-1-ylcarbonyl)phenyl]-(2-chloro-5-nitrophenyl)carboxamide showed IC50 value of 0.6 nM.

IT 172705-89-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrophenylcarboxamide derivs. as PPAR γ modulators)

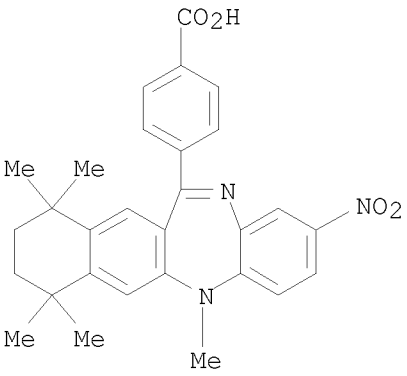
RN 172705-89-4 CAPLUS

CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 31 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:724803 CAPLUS
DOCUMENT NUMBER: 136:79548
TITLE: Inhibition of RXR and PPARγ ameliorates diet-induced obesity and type 2 diabetes
AUTHOR(S): Yamauchi, Toshimasa; Waki, Hironori; Kamon, Junji; Murakami, Koji; Motojima, Kiyoto; Komeda, Kajuro; Miki, Hiroshi; Kubota, Naoto; Terauchi, Yasuo; Tsuchida, Atsuko; Tsuboyama-Kasaoka, Nobuyo; Yamauchi, Naoko; Ide, Tomohiro; Hori, Wataru; Kato, Shigeaki; Fukayama, Masashi; Akanuma, Yasuo; Ezaki, Osamu; Itai, Akiko; Nagai, Ryozo; Kimura, Satoshi; Tobe, Kazuyuki; Kagechika, Hiroyuki; Shudo, Koichi; Kadowaki, Takashi
CORPORATE SOURCE: Department of Internal Medicine, Graduate School of Medicine, University of Tokyo, Tokyo, 113-8655, Japan
SOURCE: Journal of Clinical Investigation (2001), 108(7), 1001-1013
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PPARγ is a ligand-activated transcription factor and functions as a heterodimer with a retinoid X receptor (RXR). Supraphysiol. activation of PPARγ by thiazolidinediones can reduce insulin resistance and hyperglycemia in type 2 diabetes, but these drugs can also cause weight gain. Quite unexpectedly, a moderate reduction of PPARγ activity observed in heterozygous PPARγ-deficient mice or the Pro12Ala polymorphism in human PPARγ, has been shown to prevent insulin resistance and obesity induced by a high-fat diet. In this study, we investigated whether functional antagonism toward PPARγ/RXR could be used to treat obesity and type 2 diabetes. We show herein that an RXR antagonist and a PPARγ antagonist decrease triglyceride (TG) content in white adipose tissue, skeletal muscle, and liver. These inhibitors potentiated leptin's effects and increased fatty acid combustion and energy dissipation, thereby ameliorating HF diet-induced obesity and insulin resistance. Paradoxically, treatment of heterozygous PPARγ-deficient mice with an RXR antagonist or a PPARγ antagonist depletes white adipose tissue and markedly decreases leptin levels and energy dissipation, which increases TG content in skeletal muscle and the liver, thereby leading to the re-emergence of insulin resistance. Our data suggested that appropriate functional antagonism of PPARγ/RXR may be a logical approach to protection against obesity and related diseases such as type 2 diabetes.
IT 188844-34-0, HX 531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of RXR and PPARγ ameliorates diet-induced obesity and type 2 diabetes)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

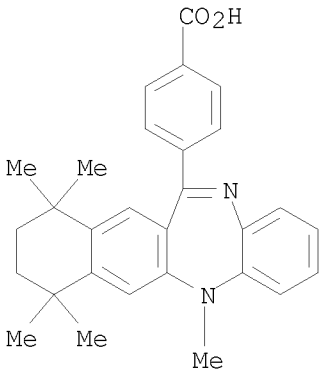


REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 32 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:169296 CAPLUS
DOCUMENT NUMBER: 134:348051
TITLE: Inhibition by retinoids of antigen-induced IL-4 production in rat mast cell line RBL-2H3
AUTHOR(S): Hirasawa, Noriyasu; Kagechika, Hiroyuki; Shudo, Koichi; Ohuchi, Kazuo
CORPORATE SOURCE: Laboratory of Pathophysiological Biochemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, 980-8578, Japan
SOURCE: Life Sciences (2001), 68(11), 1287-1294
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The retinoic acid receptor (RAR) agonists, Re80 and Am80, partially inhibited the antigen-induced IL-4 production by rat mast cell line RBL-2H3 in a concentration-dependent manner (0.1 to 100 nM). Both Re80 and Am80 also reduced the antigen-induced increase in IL-4 mRNA levels. The RAR antagonist LE540 at 4 μM reversed Re80 (100 nM)- and Am80 (100 nM)-induced inhibition of IL-4 production The retinoid X receptor agonist HX600 (1 μM) by itself did not affect IL-4 production, but enhanced the inhibitory effect of Re80 (10 nM) and of Am80 (10 nM). Cyclosporin A suppressed the antigen-induced IL-4 production almost completely at 0.3 μM. These findings indicated that the antigen-induced IL-4 production by RBL-2H3 cells is partially inhibited by retinoids via RAR-dependent mechanisms.

IT 172705-89-4, HX600
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition by retinoids of antigen-induced IL-4 production in rat mast cell line RBL-2H3)
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

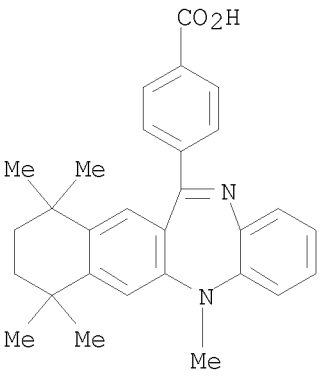


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 33 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:56245 CAPLUS
DOCUMENT NUMBER: 134:157432
TITLE: Synergistic potentiation of thiazolidinedione-induced ST 13 preadipocyte differentiation by RAR synergists
AUTHOR(S): Sato, Mayumi; Yajima, Yukiko; Kawashima, Seiichi; Tanaka, Keiji; Kagechika, Hiroyuki
CORPORATE SOURCE: Pharmaceutical Research and Development Center, Tokyo Metropolitan Institute for Medical Science, Bunkyo-ku, Tokyo, 113-8613, Japan
SOURCE: Biochemical and Biophysical Research Communications (2001), 280(3), 646-651
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peroxisome proliferator-activated receptor γ (PPAR γ) belongs to a nuclear receptor superfamily that functions as a master regulator of adipocyte differentiation. PPAR γ binds its DNA response element together with a partner, retinoid X receptor (RXR), in fat cells. Five RXR ligands (HX600, HX630, DA022, DA124, LGD1069, referred to as retinoid synergists) by themselves exhibit weak transactivation activity on the PPAR γ response element. However, addition of PPAR γ-specific ligand in this assay gave rise to a 5- to 13-fold increase, indicating a strong synergy between these ligands. LGD1069 was the most effective activator of the RXR/PPAR γ heterodimer on the transactivation of the reporter gene. But, in contrast to the other four RXR ligands, LGD1069 did not show synergistic induction of ST 13 preadipocytes to adipocytes. This apparent contradiction may result from the ligand-binding property of LGD1069. In this article the authors discuss the fact that retinoid synergists also act as PPAR γ synergists. (c) 2001 Academic Press.

IT 172705-89-4, HX600
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synergistic potentiation of thiazolidinedione-induced ST 13 preadipocyte differentiation by RAR synergists and involved mechanisms)
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 34 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:50449 CAPLUS
DOCUMENT NUMBER: 134:125954
TITLE: Use of RAR antagonists as modulators of hormone-mediated processes
INVENTOR(S): Evans, Ronald M.; Tontonoz, Peter J.; Nagy, Laszlo
PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

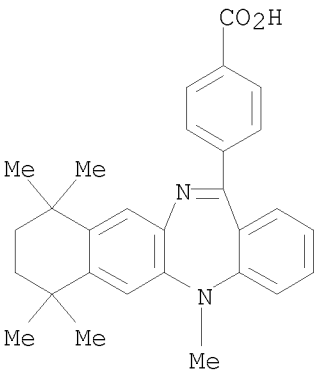
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001003659	A1	20010118	WO 2000-US18543	20000707
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6436993	B2	20020820	US 1999-352816	19990713
US 20020137794	A1	20020926		
AU 2000057878	A	20010130	AU 2000-57878	20000707

PRIORITY APPLN. INFO.: US 1999-352816 A 19990713
WO 2000-US18543 W 20000707

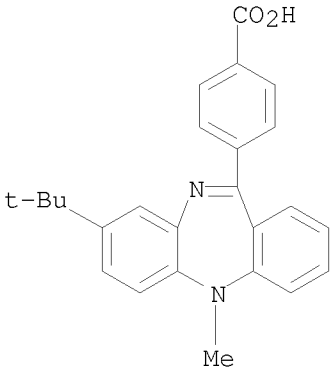
AB Retinoic acid receptor (RAR) antagonists are capable of modulating processes mediated by other members of the steroid/thyroid hormone receptor superfamily, including permissive receptors such as PPARs (e.g., PPARα, PPARδ and PPARγ). It has been discovered that RAR antagonists, in combination with agonists for members of the steroid/thyroid hormone receptor superfamily, are capable of inducing and/or enhancing processes mediated by such members.

IT 155877-83-1, LE 135
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LE 135; RAR antagonists as modulators of hormone-mediated processes)

RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



IT 203920-47-2, LE 511
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LE 511; RAR antagonists as modulators of hormone-mediated processes)
RN 203920-47-2 CAPLUS
CN Benzoic acid, 4-[8-(1,1-dimethylethyl)-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)

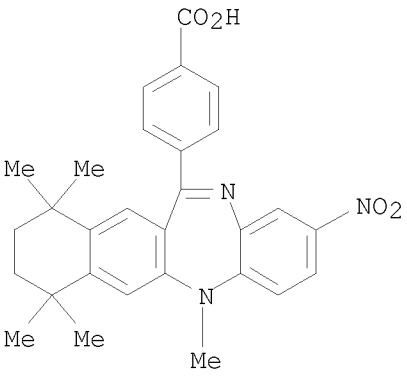


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 35 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:772398 CAPLUS
DOCUMENT NUMBER: 133:344604
TITLE: Compositions and methods using a retinoid X receptor agonist and a protein kinase A activator for treatment of hyperproliferative diseases
INVENTOR(S): Benoit, Gerard; Gronemeyer, Hinrich; Lanotte, Michel; Gottardis, Marco
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Institut National de la Sante et de la Recherche Medicale; Centre National de la Recherche Scientifique; Universite Louis Pasteur
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064260	A1	20001102	WO 1999-US8908	19990423
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2369910	A1	20001102	CA 1999-2369910	19990423
AU 9941815	A1	20001110	AU 1999-41815	19990423
AU 773928	B2	20040610		
EP 1173061	A1	20020123	EP 1999-925558	19990423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002542268	T	20021210	JP 2000-613263	19990423
PRIORITY APPLN. INFO.:			WO 1999-US8908 W	19990423

AB The invention provides compns. comprising a retinoid X receptor agonist and an agent capable of activating protein kinase A. The invention also provides methods of treating hyperproliferative diseases by administering a retinoid X receptor agonist and an agent capable of activating protein kinase A.
IT 188844-34-0, HX 531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(HX 531; retinoid X receptor agonist and protein kinase A activator for treatment of hyperproliferative disease)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

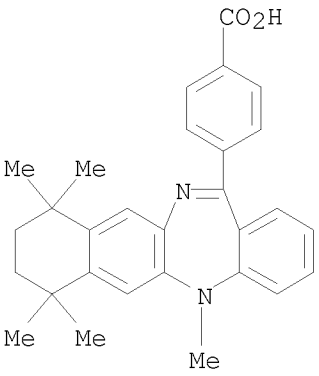


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

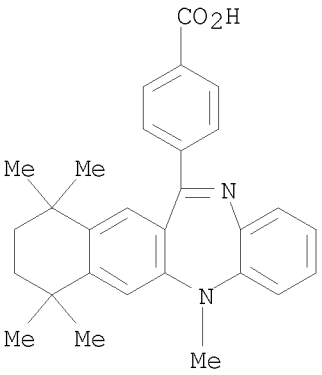
L25 ANSWER 36 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:307979 CAPLUS
DOCUMENT NUMBER: 133:202727
TITLE: Identification of receptor-selective retinoids that are potent inhibitors of the growth of human head and neck squamous cell carcinoma cells
AUTHOR(S): Sun, Shi-Yong; Yue, Ping; Mao, Li; Dawson, Marcia I.; Shroot, Braham; Lamph, William W.; Heyman, Richard A.; Chandraratna, Roshantha A. S.; Shudo, Koichi; Hong, Waun K.; Lotan, Reuben
CORPORATE SOURCE: Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Clinical Cancer Research (2000), 6(4), 1563-1573
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Retinoids modulate the growth and differentiation of cancer cells presumably by activating gene transcription via the nuclear retinoic acid receptor (RAR) α, β, and γ and retinoid X receptor (RXR) α, β, and γ. We analyzed the effects of 38 RAR-selective and RXR-selective retinoids on the proliferation of 10 human head and neck squamous cell carcinoma (HNSCC) cell lines. All of these cell lines expressed constitutively all of the receptor subtypes except RARβ, which was detected in only two of them. Most of the RAR-selective retinoids inhibited the growth of HNSCC cells to varying degrees, whereas the RXR-selective retinoids showed very weak or no inhibitory effects. Three RAR antagonists suppressed growth inhibition by RAR-selective agonists, as well as by RAR/RXR antagonists such as 9-cis-retinoic acid. Combinations of RXR-selective and RAR-selective retinoids exhibited additive growth-inhibitory effects. Furthermore, we found that CD437, the most potent growth-inhibitory retinoid induced apoptosis and up-regulated the expression of several apoptosis-related genes in HNSCC cells. These results indicate that: (a) retinoid receptors are involved in the growth-inhibitory effects of retinoids; (b) RXR-RAR heterodimers rather than RXR-RXR homodimer are the major mediators of growth inhibition by retinoids in HNSCC cells; and (c) induction of apoptosis can account for one mechanism by which retinoids such as CD437 inhibit the growth of HNSCC cells. Finally, these studies identified several synthetic retinoids, which are much more effective than the natural RAs and can be good candidates for chemoprevention and therapy of head and neck cancers.

IT 155877-83-1, LE 135
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LE 135; receptor-selective retinoids as inhibitors of human head and neck squamous cell carcinoma cells)
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)

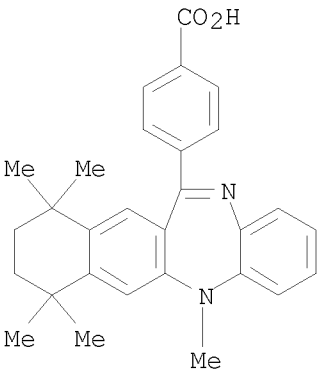


IT 172705-89-4, HX600
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(receptor-selective retinoids as inhibitors of human head and neck squamous cell carcinoma cells)
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

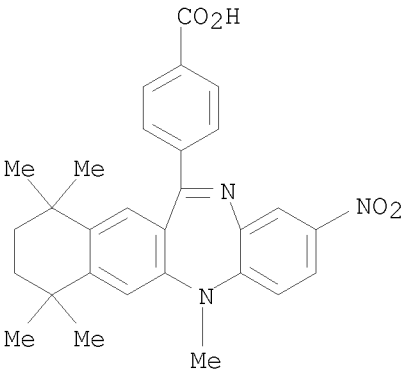


REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

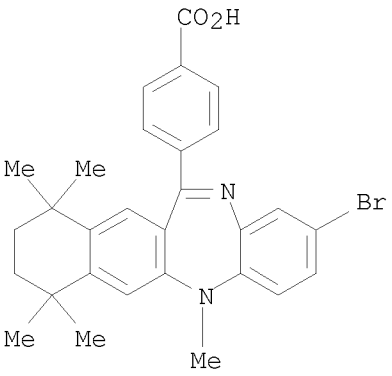
L25 ANSWER 37 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:2279 CAPLUS
DOCUMENT NUMBER: 132:175327
TITLE: Retinoid X receptor-antagonistic diazepinylbenzoic acids
AUTHOR(S): Ebisawa, Masayuki; Umemiya, Hiroki; Ohta, Kiminori; Fukasawa, Hiroshi; Kawachi, Emiko; Christoffel, Ghislaine; Gronemeyer, Hinrich; Tsuji, Motonori; Hashimoto, Yuichi; Shudo, Koichi; Kagechika, Hiroyuki
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, University of Tokyo, Tokyo, 113-0033, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1999), 47(12), 1778-1786
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several dibenzodiazepine derivs. were identified as novel retinoid X receptor (RXR) antagonists on the basis of inhibitory activity on retinoid-induced cell differentiation of human promyelocytic leukemia cells HL-60 and transactivation assay using retinoic acid receptors (RARs) and RXRs in COS-1 cells. 4-(5H-2,3-(2,5-Dimethyl-2,5-hexano)-5-n-propyldibenzo[b,e][1,4]diazepin-11-yl)benzoic acid (HX603) is an N-Pr derivative of an RXR pan-agonist HX600, and exhibited RXR-selective antagonistic activity. Similar RXR-antagonistic activities were observed with 4-(5H-2,3-(2,5-dimethyl-2,5-hexano)-5-methyl-8-nitrodibenzo[b,e][1,4]diazepin-11-yl)benzoic acid (HX531) and 4-(5H-10,11-dihydro-5,10-dimethyl-2,3-(2,5-dimethyl-2,5-hexano)-dibenzo[b,e][1,4]diazepin-11-yl)benzoic acid (HX711), which also inhibited transactivation of RARs induced by an RAR agonist, Am80. These compds. inhibited HL-60 cell differentiation induced by the combination of a low concentration of the retinoid agonist Am80 with an RXR agonist (a retinoid synergist, HX600). These results indicated that HX603 and the related RXR antagonists inhibit the activation of RAR-RXR heterodimers as well as RXR homodimers, which is a distinct characteristic different from that of the known RXR antagonist, LG100754.
IT 172705-89-4, HX600
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and biol. activity of dibenzodiazepine derivs. as retinoid X receptor antagonists)
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



IT 188844-34-0P, HX 531 259228-78-9P, HX 539
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. activity of dibenzodiazepine derivs. as retinoid X receptor antagonists)
RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

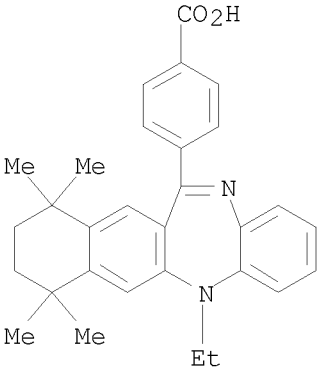


RN 259228-78-9 CAPLUS
CN Benzoic acid, 4-(2-bromo-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

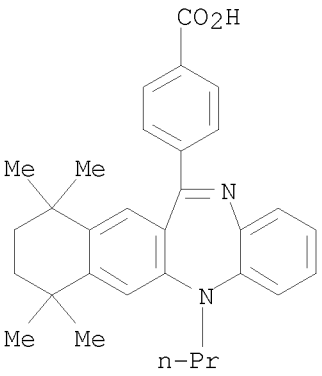


IT 259228-71-2P, HX 602 259228-72-3P, HX 603
259228-73-4P, HX 604 259228-74-5P, HX 605
259228-75-6P, HX 607 259228-76-7P, HX 533
259228-77-8P, HX 535 259228-79-0P, HX 541
259228-80-3P, HX 543 259228-81-4P, HX 560
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of dibenzodiazepine derivs. as retinoid X receptor antagonists)

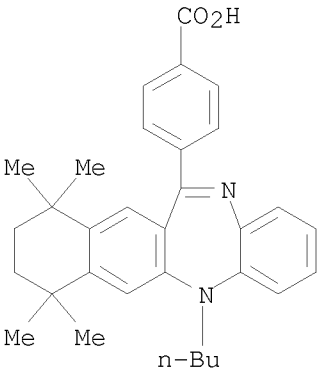
RN 259228-71-2 CAPLUS
CN Benzoic acid, 4-(5-ethyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



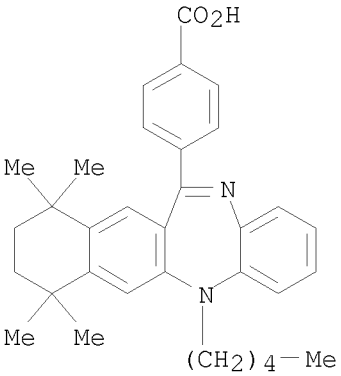
RN 259228-72-3 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-propyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



RN 259228-73-4 CAPLUS
CN Benzoic acid, 4-(5-butyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

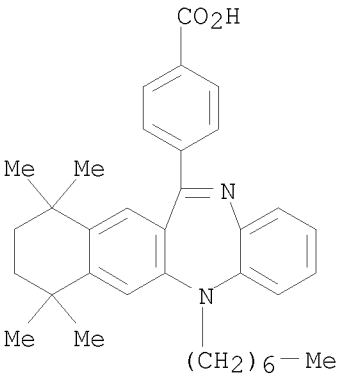


RN 259228-74-5 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-pentyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

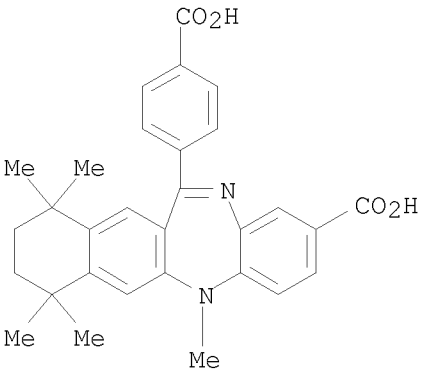


RN 259228-75-6 CAPLUS

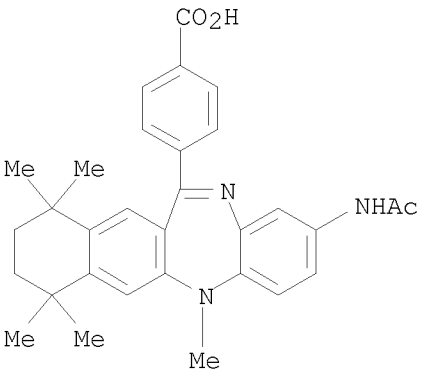
CN Benzoic acid, 4-(5-heptyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



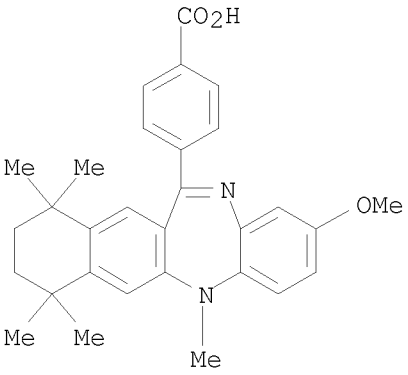
RN 259228-76-7 CAPLUS
CN 5H-Benzo[b]naphtho[2,3-e][1,4]diazepine-2-carboxylic acid, 12-(4-carboxyphenyl)-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl- (CA INDEX NAME)



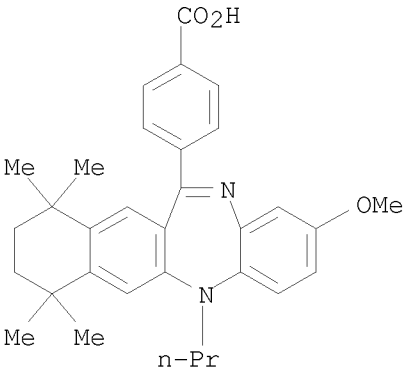
RN 259228-77-8 CAPLUS
CN Benzoic acid, 4-[2-(acetylamino)-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]- (CA INDEX NAME)



RN 259228-79-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-2-methoxy-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

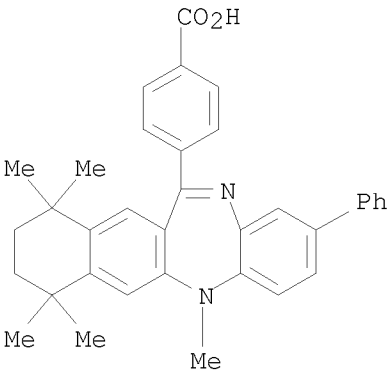


RN 259228-80-3 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-2-methoxy-7,7,10,10-tetramethyl-5-propyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



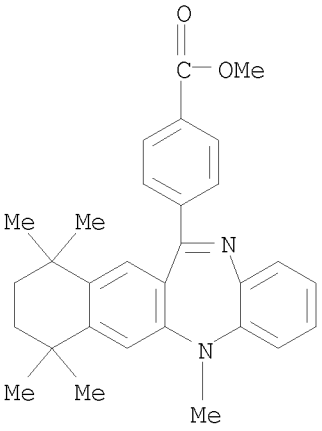
RN 259228-81-4 CAPLUS

CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-phenyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

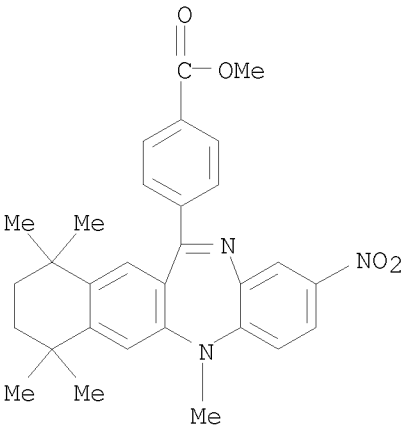


IT 188844-81-7P 188845-12-7P 259219-29-9P
259219-30-2P 259219-31-3P 259219-32-4P
259219-33-5P 259219-34-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. activity of dibenzodiazepine derivs. as retinoid X receptor antagonists)

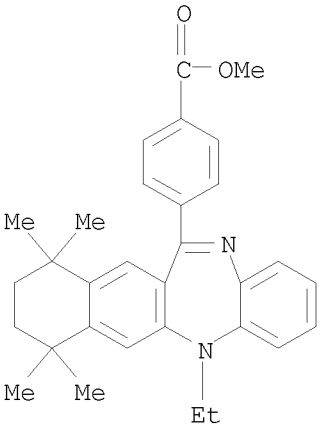
RN 188844-81-7 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



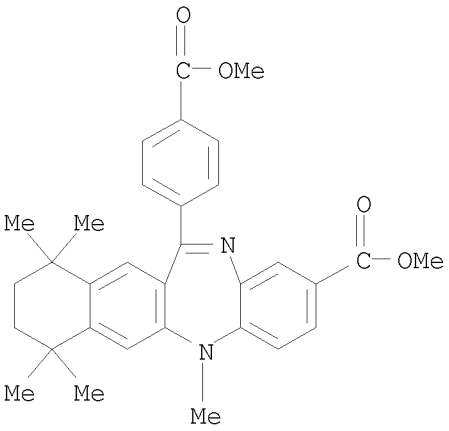
RN 188845-12-7 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



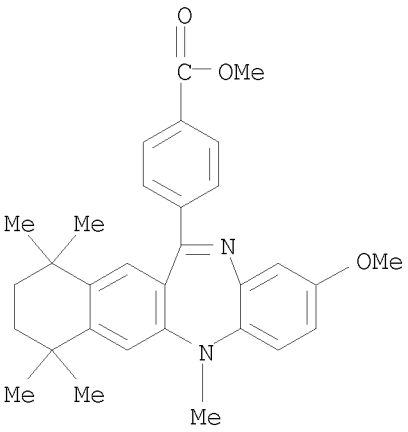
RN 259219-29-9 CAPLUS
CN Benzoic acid, 4-(5-ethyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



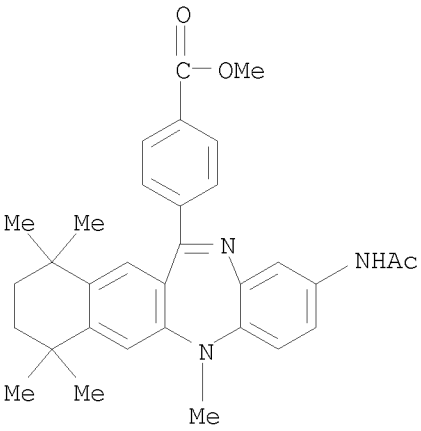
RN 259219-30-2 CAPLUS
CN 5H-Benzo[b]naphtho[2,3-e][1,4]diazepine-2-carboxylic acid, 7,8,9,10-tetrahydro-12-[4-(methoxycarbonyl)phenyl]-5,7,7,10,10-pentamethyl-, methyl ester (CA INDEX NAME)



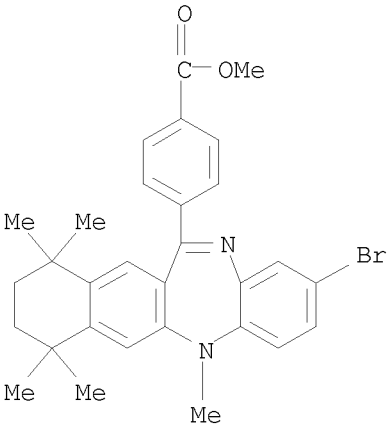
RN 259219-31-3 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-2-methoxy-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



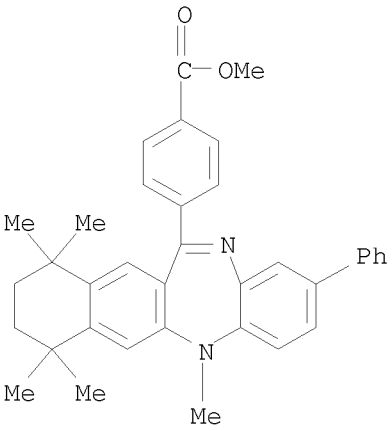
RN 259219-32-4 CAPLUS
CN Benzoic acid, 4-[2-(acetylamino)-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl]-, methyl ester (CA INDEX NAME)



RN 259219-33-5 CAPLUS
CN Benzoic acid, 4-(2-bromo-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



RN 259219-34-6 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-phenyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 38 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:736508 CAPLUS
DOCUMENT NUMBER: 131:356081
TITLE: Formulations useful for modulating expression of exogenous genes in mammalian systems, and products related thereto
INVENTOR(S): Evans, Ronald M.; Saez, Enrique
PATENT ASSIGNEE(S): Salk Institute for Biological Studies, USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

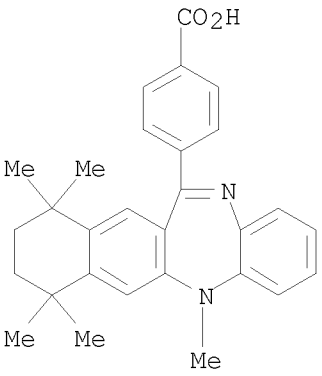
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958155	A1	19991118	WO 1999-US8381	19990416
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6333318	B1	20011225	US 1998-79570	19980514
CA 2328521	A1	19991118	CA 1999-2328521	19990416
AU 9936486	A	19991129	AU 1999-36486	19990416
AU 759521	B2	20030417		
EP 1076569	A1	20010221	EP 1999-918614	19990416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002514609	T	20020521	JP 2000-548006	19990416
US 20020187972	A1	20021212	US 2001-949278	20010907
US 7045315	B2	20060516		

PRIORITY APPLN. INFO.: US 1998-79570 A1 19980514
WO 1999-US8381 W 19990416
OTHER SOURCE(S): MARPAT 131:356081

AB In accordance with the present invention, there are provided various methods for modulating the expression of an exogenous gene in a mammalian subject employing modified ecdysone receptors. Also provided are modified ecdysone receptors, as well as homomeric and heterodimeric receptors containing same, nucleic acids encoding invention modified ecdysone receptors, modified hormone response elements, gene transfer vectors, recombinant cells, and transgenic animals containing nucleic acids encoding invention modified ecdysone receptor.

IT 172705-89-4
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ecdysone receptor systems for modulating expression of exogenous genes in mammalian systems)

RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

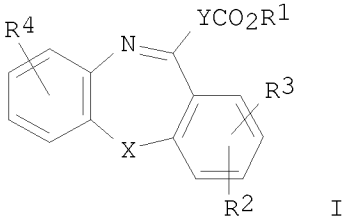


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

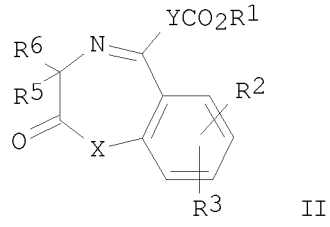
L25 ANSWER 39 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:390380 CAPLUS
DOCUMENT NUMBER: 131:39745
TITLE: Benzodiazepine derivatives as preventives/remedies for diabetes
INVENTOR(S): Kagechika, Hiroyuki; Hashimoto, Yuichi; Fujii, Hideji; Yonekawa, Yoshiaki; Ekimoto, Hisao
PATENT ASSIGNEE(S): Institute of Medicinal Molecular Design. Inc., Japan
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9929324	A1	19990617	WO 1998-JP5480		19981204
W: AU, CA, CN, ID, KR, NO, SG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
JP 11171776	A	19990629	JP 1997-335956		19971205
CA 2312716	A1	19990617	CA 1998-2312716		19981204
AU 9913520	A	19990628	AU 1999-13520		19981204
EP 1036565	A1	20000920	EP 1998-957170		19981204
R: CH, DE, FR, GB, IT, LI					
US 6458782	B1	20021001	US 2000-555508		20000901
PRIORITY APPLN. INFO.:			JP 1997-335956	A	19971205
			WO 1998-JP5480	W	19981204

OTHER SOURCE(S): MARPAT 131:39745
GI



I



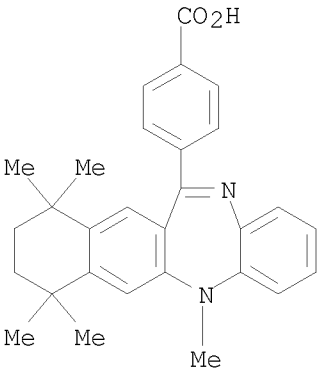
II

AB Benzodiazepine derivs. containing as the active ingredient compds. represented

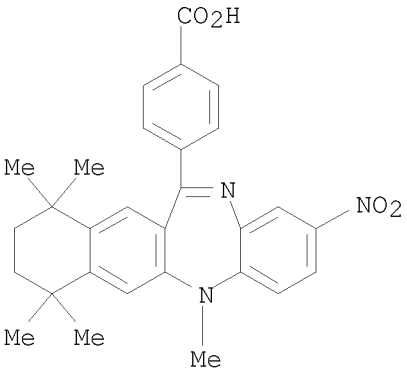
by general formula (I and II) and being useful in preventing and treating diabetes and complication thereof, wherein R1 represents hydrogen or C1-6 alkyl; R2 and R3 represent each hydrogen or C1-6 alkyl, or R2 and R3 may form together with the carbon atom on the Ph ring to which they are bonded a 5- or 6-membered ring; R4 represents hydrogen, C1-6 alkyl, C1-6 alkoxy, etc.; R6 represents hydrogen or C1-6 alkyl; X represents -NR7-, -NO-, -O-, etc. (wherein R7 represents hydrogen, C1-6 alkyl, etc.); and Y represents phenylene or pyridinediyl. I and II are claimed as oral antidiabetics and hypolipidemics and have synergistic effect with other antidiabetics.

IT 172705-89-4, HX600 188844-34-0, HX 531
203920-36-9, HX 610 203920-47-2, HX 511
227328-77-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzodiazepine derivs. as preventives/remedies for diabetes)

RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

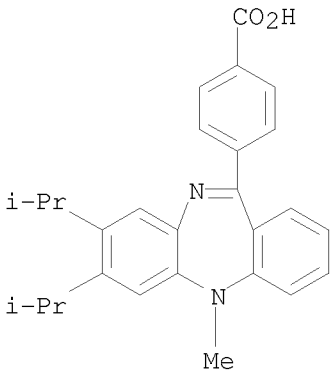


RN 188844-34-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

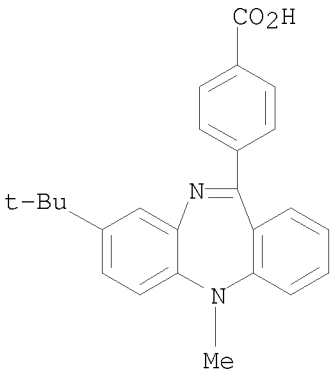


RN 203920-36-9 CAPLUS

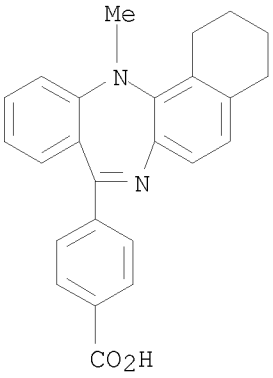
CN Benzoic acid, 4-[5-methyl-7,8-bis(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



RN 203920-47-2 CAPLUS
CN Benzoic acid, 4-[8-(1,1-dimethylethyl)-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)

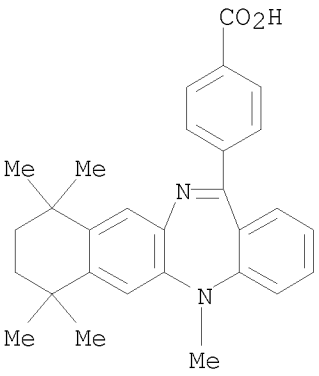


RN 227328-77-0 CAPLUS
CN Benzoic acid, 4-(2,3,4,13-tetrahydro-13-methyl-1H-benzo[e]naphtho[2,1-b][1,4]diazepin-8-yl)- (CA INDEX NAME)

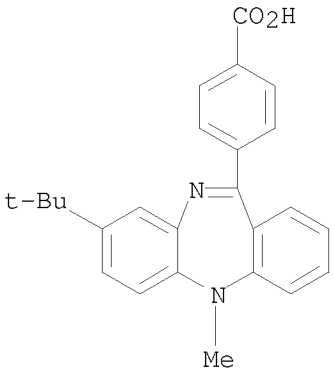


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 40 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:349303 CAPLUS
DOCUMENT NUMBER: 131:125431
TITLE: Identification of a novel class of retinoic acid receptor β-selective retinoid antagonists and their inhibitory effects on AP-1 activity and retinoic acid-induced apoptosis in human breast cancer cells
AUTHOR(S): Li, Yin; Hashimoto, Yuichi; Agadir, Anissa; Kagechika, Hiroyuki; Zhang, Xiao-Kun
CORPORATE SOURCE: Cancer Research Center, Burnham Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of Biological Chemistry (1999), 274(22), 15360-15366
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Four candidate retinoid antagonists (LE135, LE511, LE540, and LE550) were designed on the basis of the ligand superfamily concept and synthesized. Anal. of these related retinoids by transient transfection assay demonstrated that LE135, LE540, and LE550 are effective retinoic acid receptor (RAR) antagonists, whereas LE511 selectively induced RARβ transcriptional activity. Both LE135 and LE540 inhibited retinoic acid (RA)-induced transcriptional activation of RARβ, but not RARα, RARγ or retinoid X receptor α (RXRα), on a variety of RA response elements. The retinoid antagonists also inhibited all-trans-RA-induced transcriptional activation of RARβ/RXRα heterodimers, although they did not show any effect on transactivation activity of RXR/RXR homodimers. In ZR-75-1 human breast cancer cells, cotreatment of LE135 and LE540 with all-trans-RA inhibited all-trans-RA-induced apoptosis of the cells, further demonstrating that RARβ plays a role in RA-induced apoptosis of breast cancer cells. We also evaluated the effect of these retinoids on AP-1 activity. Our data showed that LE135 and LE540 strongly repressed 12-O-tetradecanoylphorbol-13-acetate-induced AP-1 activity in the presence of RARβ and RXRα. Interestingly, LE550 induced AP-1 activity when RARβ and RXRα were expressed in HeLa cells but not in breast cancer cells. These results demonstrate that LE135 and LE540 were a novel class of RARβ-selective antagonists and anti-AP-1 retinoids and should be useful tools for studying the role of retinoids and their receptors.
IT 155877-83-1, LE 135 203920-47-2, LE 511
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(retinoic acid receptor β-selective retinoid antagonists and their inhibitory effects on AP-1 activity and retinoic acid-induced apoptosis in human breast cancer cells)
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



RN 203920-47-2 CAPLUS
CN Benzoic acid, 4-[8-(1,1-dimethylethyl)-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 41 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:325919 CAPLUS
DOCUMENT NUMBER: 130:352284
TITLE: Preparation of 5-benzylidenethiazolidine-2,4-dione and 10-[4-[(2,4-dioxothiazolidin-5-ylidene)methyl]phenyl]-5H-dibenzo[b,e][1,4]diazepine derivatives as retinoid receptor agonists
INVENTOR(S): Kagechika, Hiroyuki; Hashimoto, Yuichi; Itai, Akiko
PATENT ASSIGNEE(S): Institute of Medicinal Molecular Design, Inc., Japan
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9924415	A1	19990520	WO 1998-JP5091		19981112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2309331	A1	19990520	CA 1998-2309331		19981112
AU 9910525	A	19990531	AU 1999-10525		19981112
EP 1048659	A1	20001102	EP 1998-953024		19981112
R: CH, DE, FR, GB, IT, LI					
PRIORITY APPLN. INFO.:			JP 1997-310835	A	19971112
			WO 1998-JP5091	W	19981112

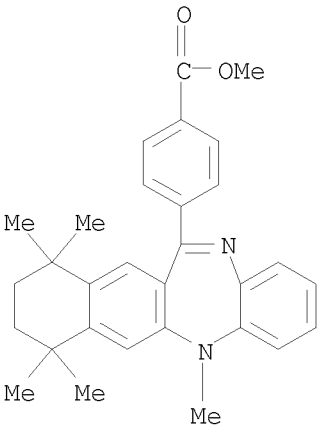
OTHER SOURCE(S): MARPAT 130:352284
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

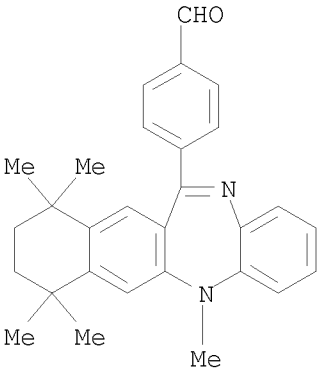
AB The title compds. (I; R1-R5 = H or lower alkyl or adjacent 2 groups of R1-R5 form together with the carbon atoms of the Ph ring to from 5- to 6-membered ring optionally 1 or ≥2 alkyl groups; X = CR6:CH, CH:CR7, NR8CO, CONR9, C(:CHR10), CO, or NR11; R6-R11 = H lower alkyl) and (II; R21-R24 = H or lower alkyl or adjacent 2 groups of R1-R5 form together with the carbon atoms of the Ph ring to from 5- to 6-membered ring optionally 1 or ≥2 alkyl groups; R25 = H, lower alkyl), which are retinoid receptor agonists having retinoic effects or regulatory effects of increasing or suppressing retinoid actions, are prepared These compds. are useful for the prevention and/or treatment of cancers, diabetes, arteriosclerosis, bone diseases, rheumatism, and autoimmune diseases. Thus, 4-[1-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-yl)vinyl]benzaldehyde was condensed with 2,4-thiazolidinedione in the presence of piperidine and AcOH in toluene under reflux at 120° to give the title compound (III). III in vitro promoted the differentiation of HL-60 cell to granulocyte by 2.8, 6.4, and 89% at 10-8, 10-7 and 10-6 M,

resp., and 76, and 84, and 92% in the copresence of 3+10-9 M Am80, resp.

IT 188844-81-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzylidenethiazolidinedione and [[(dioxothiazolidinylidene)methyl]phenyl]-5H-dibenzo[b,e][1,4]diazepine derivs. as retinoid receptor agonists as preventives and therapeutics)
RN 188844-81-7 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



IT 224630-17-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzylidenethiazolidinedione and [[(dioxothiazolidinylidene)methyl]phenyl]-5H-dibenzo[b,e][1,4]diazepine derivs. as retinoid receptor agonists as preventives and therapeutics)
RN 224630-17-5 CAPLUS
CN Benzaldehyde, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

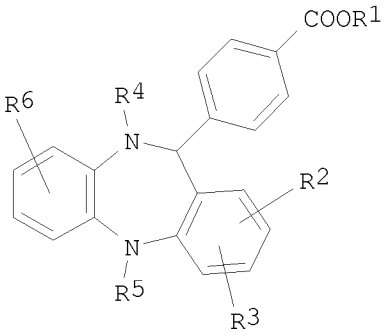


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 42 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:274903 CAPLUS
DOCUMENT NUMBER: 129:36446
ORIGINAL REFERENCE NO.: 129:7529a,7532a
TITLE: (Dibenzodiazepinyl)benzoic acids, retinoid antagonists, and pharmaceuticals containing them
INVENTOR(S): Shudo, Koichi
PATENT ASSIGNEE(S): Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10114757	A	19980506	JP 1996-269649	19961011
JP 4005160	B2	20071107		

PRIORITY APPLN. INFO.: JP 1996-269649 19961011
OTHER SOURCE(S): MARPAT 129:36446
GI

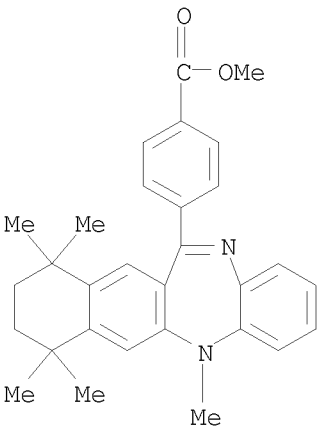


I

AB Retinoid antagonists comprise title compds. I (R1-R5 = H, C1-6 alkyl; R2R3 may form 5- or 6-membered cycloalkyl ring; R6 = H, C1-6 alkyl, C1-6 alkoxy, OH, NO2, halo) or their salts. I are useful for treatment of hypervitaminosis, cancer, diabetes mellitus, arteriosclerosis, bone diseases, rheumatism, and immune diseases. HX711 [I (R1 = R6 = H, R2R3 = CMe2CH2CH2CMe2, R4 = R5 = Me)] was prepared from Me 4-[5H-5-methyl-7,8-(2,5-dimethyl-2,5-hexano)dibenzo[b,e]diazepin-10-yl]benzoate (preparation given) in 3 steps. Antagonistic activity of HX711 was shown in Am80-induced cell differentiation.

IT 188844-81-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (dibenzodiazepinyl)benzoic acids as retinoid antagonists)

RN 188844-81-7 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)


O
C
OMe
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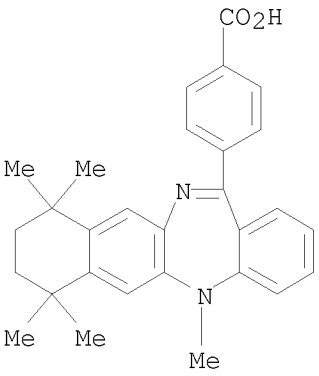
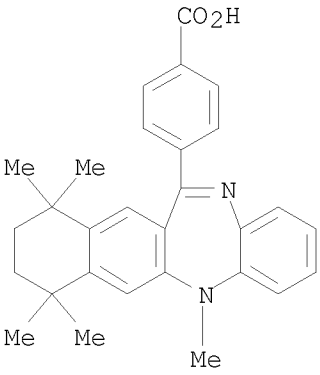
Me
Me

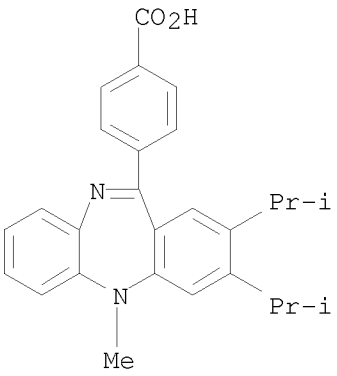
L25 ANSWER 43 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:35362 CAPLUS
DOCUMENT NUMBER: 128:200541
ORIGINAL REFERENCE NO.: 128:39483a,39486a
TITLE: Retinobenzoic acids. VIII. Regulation of retinoidal actions by diazepinylbenzoic acids. Retinoid synergists which activate the RXR-RAR heterodimers
AUTHOR(S): Umemiya, Hiroki; Fukasawa, Hiroshi; Ebisawa, Masayuki; Eyrolles, Laurence; Kawachi, Emiko; Eisenmann, Ghislaine; Gronemeyer, Hinrich; Hoshimoto, Yuichi; Shudo, Koichi; Kagechika, Hiroyuki
CORPORATE SOURCE: Graduate School Pharmaceutical Sci., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Journal of Medicinal Chemistry (1997), 40(26), 4222-4234
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In human HL-60 promyelocytic leukemia cells, diazepinylbenzoic acid derivs. can exhibit either antagonistic or synergistic effects on the differentiation-inducing activities of natural or synthetic retinoids, the activity depending largely on the nature of the substituents on the diazepine ring. Thus, a benzolog of the retinoid antagonist LE135 (6), 4-(13H-10,11,12,13-tetrahydro-10,10,13,13,15-pentamethyldinaphtho[2,3-b][1,2-e]diazepin-7-yl)benzoic acid (LE540), exhibits a 1 order of magnitude higher antagonistic potential than the parental LE135. In contrast, 4-[5H-2,3-(2,5-dimethyl-2,5-hexano)-5-methyldibenzo[b,e][1,4]diazepin-11-yl]-benzoic acid (HX600), a structural isomer of the antagonistic LE135, enhanced HL-60 cell differentiation induced by RAR agonists, such as Am80. This synergistic effect was further increased for a thiazepine, HX630, and an azepine derivative, HX640; both synergized with Am80 more potently than HX600. Notably, the neg. and pos. effects of the azepine derivs. on retinoidal actions can be related to their RAR-antagonistic and RXR-agonistic properties, resp., in the context of the RAR-RXR heterodimer.
IT 155877-83-1, LE 135 172705-89-4, HX600
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(retinoid synergists which activate the RXR-RAR heterodimers)
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



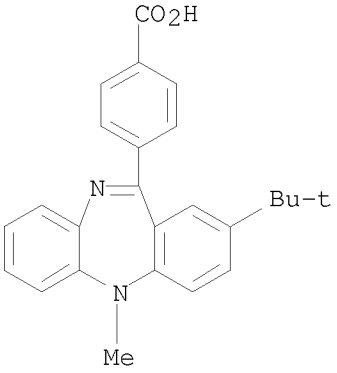
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



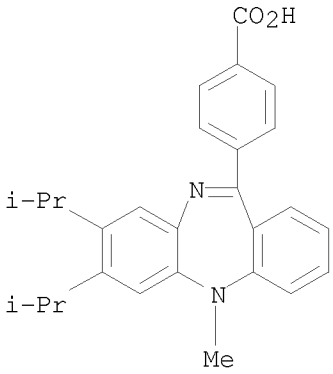
IT 188844-28-2P 188844-31-7P 203920-36-9P
203920-38-1P 203920-43-8P 203920-47-2P
203920-48-3P 203920-49-4P 203920-50-7P
203920-51-8P 203920-52-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(retinoid synergists which activate the RXR-RAR heterodimers)
RN 188844-28-2 CAPLUS
CN Benzoic acid, 4-[5-methyl-2,3-bis(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



RN 188844-31-7 CAPLUS
CN Benzoic acid, 4-[2-(1,1-dimethylethyl)-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)

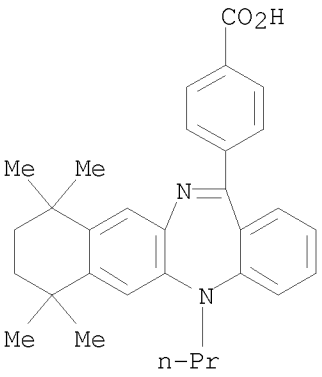


RN 203920-36-9 CAPLUS
CN Benzoic acid, 4-[5-methyl-7,8-bis(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



RN 203920-38-1 CAPLUS

CN Benzoic acid, 4-(7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5-propyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



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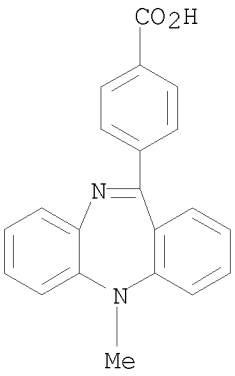
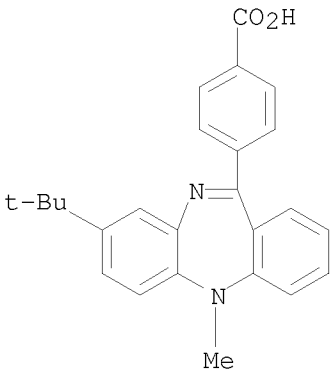
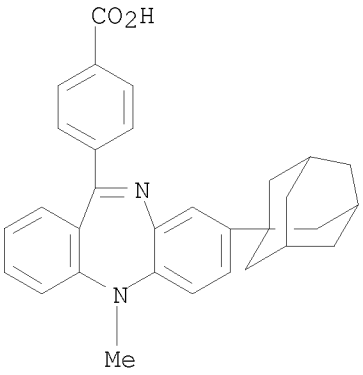


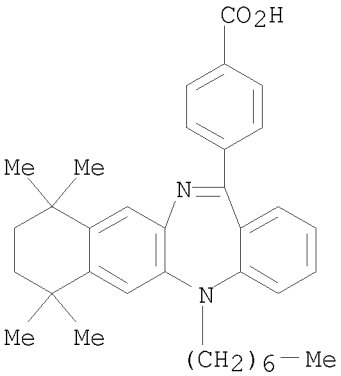
RN 203920-47-2 CAPLUS
CN Benzoic acid, 4-[8-(1,1-dimethylethyl)-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)



RN 203920-48-3 CAPLUS
CN Benzoic acid, 4-(5-methyl-8-tricyclo[3.3.1.13,7]dec-1-yl-5H-dibenzo[b,e][1,4]diazepin-11-yl)- (CA INDEX NAME)

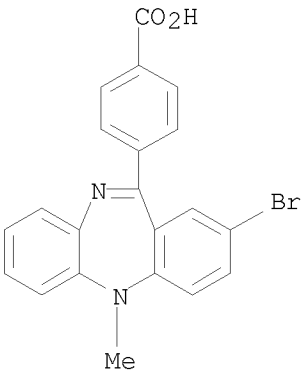


RN 203920-49-4 CAPLUS
CN Benzoic acid, 4-(5-heptyl-7,8,9,10-tetrahydro-7,7,10,10-tetramethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)

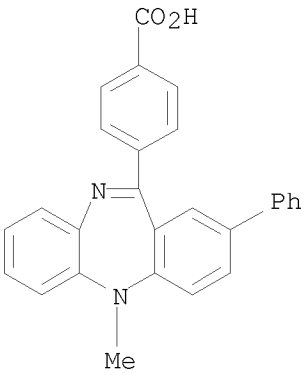


RN 203920-50-7 CAPLUS

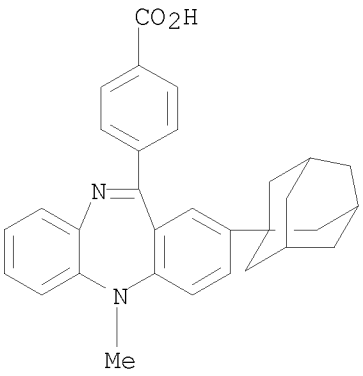
CN Benzoic acid, 4-(2-bromo-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl)-
(CA INDEX NAME)



RN 203920-51-8 CAPLUS
CN Benzoic acid, 4-(5-methyl-2-phenyl-5H-dibenzo[b,e][1,4]diazepin-11-yl)-
(CA INDEX NAME)



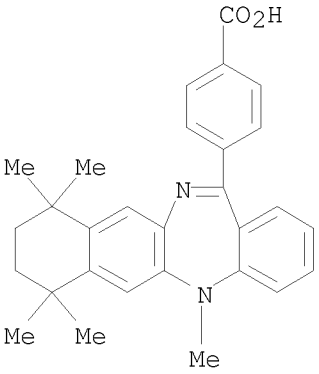
RN 203920-52-9 CAPLUS
CN Benzoic acid, 4-(5-methyl-2-tricyclo[3.3.1.13,7]dec-1-yl-5H-
dibenzo[b,e][1,4]diazepin-11-yl)- (CA INDEX NAME)



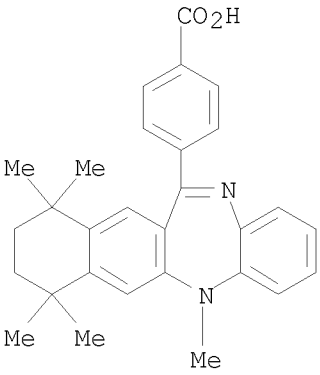
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 44 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:729413 CAPLUS
DOCUMENT NUMBER: 128:43515
ORIGINAL REFERENCE NO.: 128:8375a,8378a
TITLE: Differential effects of synthetic nuclear retinoid receptor-selective retinoids on the growth of human non-small cell lung carcinoma cells
AUTHOR(S): Sun, Shi-Yong; Yue, Ping; Dawson, Marcia I.; Shroot, Braham; Michel, Serge; Lamph, William W.; Heyman, Richard A.; Teng, Min; Chandraratna, Roshantha A. S.; Shudo, Koichi; Hong, Waun K.; Lotan, Reuben
CORPORATE SOURCE: Department of Tumor Biology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Cancer Research (1997), 57(21), 4931-4939
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retinoids are promising agents for cancer chemoprevention and therapy. Nuclear retinoic acid receptors (RARs; RARα, -β, and -γ) and retinoid X receptors (RXRs; RXRα, -β, and -γ) are thought to mediate most of retinoids' effects on cell growth and differentiation. Because the majority of human non-small cell lung carcinoma (NSCLC) cell lines are resistant to all-trans-retinoic acid, the authors searched for more potent retinoids. Therefore, the authors examined the effects of 37 natural and synthetic retinoids that exhibit specific binding to and transactivation of individual RARs or RXRs on the proliferation of eight human NSCLC cell lines. All of these cells expressed mRNAs of the three RXRs; however, they expressed varying levels of RARα and RARγ, and only three of the eight cell lines expressed RARβ mRNA. Cellular retinoic acid-binding proteins (CRABPs) I and II were detected in one and three of the eight cell lines, resp. Only 8 of the 37 retinoids exhibited growth-inhibitory activity (IC50, <10 μM) against at least two of the eight NSCLC cell lines. The active retinoids included one (TD550) of five RARα-selective, one (Ch55) of three RARβ-selective, three (CD437, CD2325, and SR11364) of six RARγ-selective, and one (CD271) of four RARβ/γ-selective retinoids. The potency of these retinoids was low (IC50, > 1 μM), except for CD437, which was very potent (IC50, 0.1-0.5 μM). The six RXR-selective retinoids were mostly inactive even at 10 μM. However, combinations of RAR-selective and RXR-selective retinoids exhibited additive effects. There appeared to be no simple correlation among the histol. type of the NSCLC (adeno- or squamous), the levels of nuclear receptors or CRABPs, and the response of the cells to the growth-inhibitory effects of retinoids. Nevertheless, in contrast with former studies with natural retinoids, these results suggest that several synthetic retinoids do exhibit inhibitory activity against NSCLC cells, and some of them may be useful clin.
IT 155877-83-1, LE 135 172705-89-4, HX600
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential effects of synthetic nuclear retinoid receptor-selective retinoids on growth of human non-small cell lung carcinoma cells in relation to receptor and retinoic acid-binding protein expression)
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-

benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



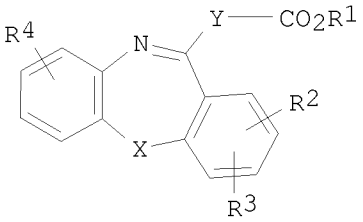
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 45 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:286725 CAPLUS
DOCUMENT NUMBER: 126:264112
ORIGINAL REFERENCE NO.: 126:51157a,51160a
TITLE: Preparation of (di)benzodiazepine, (di)benzothiazepine, and (di)benzoxazepine compounds potentiating retinoid
INVENTOR(S): Shudo, Koichi
PATENT ASSIGNEE(S): Nikken Chemicals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

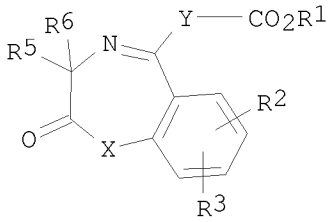
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9711061	A1	19970327	WO 1996-JP2709	19960920
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 10059951	A	19980303	JP 1996-245965	19960918
JP 3865829	B2	20070110		
CA 2233012	A1	19970327	CA 1996-2233012	19960920
AU 9670015	A	19970409	AU 1996-70015	19960920
CN 1202160	A	19981216	CN 1996-198386	19960920
CN 1121395	C	20030917		
EP 906907	A1	19990407	EP 1996-931263	19960920
EP 906907	B1	20020306		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, FI				
US 5929069	A	19990727	US 1996-710657	19960920
TW 420667	B	20010201	TW 1996-85111550	19960920
AT 214055	T	20020315	AT 1996-931263	19960920
NO 9801269	A	19980520	NO 1998-1269	19980320
US 6121256	A	20000919	US 1999-288618	19990409
US 20010039272	A1	20011108	US 2001-838272	20010420
US 6476017	B2	20021105		

PRIORITY APPLN. INFO.:	JP 1995-242639	A	19950921
	JP 1996-150582	A	19960612
	US 1996-710657	A3	19960920
	WO 1996-JP2709	W	19960920
	US 1999-288618	A3	19990409
	US 2000-626449	B1	20000726

OTHER SOURCE(S): MARPAT 126:264112
GI



I



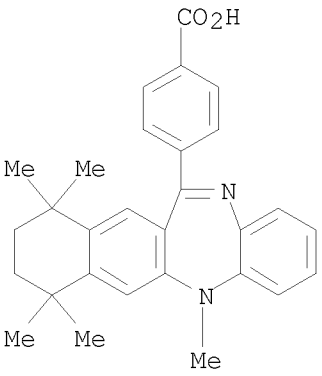
II

AB Compds. represented by general formula (I or II; R1 - R3 = H or C1-6 alkyl; or R2 and R3 together form 5- or 6-membered cycloalkyl; R4 = H, C1-6 alkyl, C1-6 alkoxy, OH, NO2, halo; R5 = H, C1-6 alkyl, aryl-C1-6 alkyl; R6 = H, C1-6 alkyl; X = NR7, O, CHR7 or S; wherein R7 = H, C1-6 alkyl, aryl-C1-6 alkyl; Y = phenylene, pyridinediyl) or salts thereof which potentiate biol. activities of internuclear receptor ligands typified by retinoic acid or retinoids having retinoic acid-like activities, are prepared Claimed is an enhancer for the effect of biol. substances which exhibit the biol. activities by binding to a super family of internuclear receptors using above compds. I and II. Also claimed is a method for enhancing the effect of biol. substances which exhibit the biol. activates by binding to a super family of internuclear receptors, by administering above compds. I and II to mammals. Thus, 6-bromo-1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalene was condensed with o-nitroaniline in the presence of K2CO3 and CuI in xylene under reflux for 24 h to give 6-(o-nitroanilino)-1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalene, which was reduced by Fe/HCl in aqueous EtOH to 6-(o-aminoanilino)-1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalene. The latter compound was amidated with p-MeO2CC6H4COCl in the presence of pyridine in benzene at room temperature for 3 h to give 6-[2-(4-methoxycarbonylbenzoylamino)anilino]-1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalene, which was stirred in polyphosphoric acid at 120° for 1 h to give a dibenzo[b,e]diazepine (III; R = Me). This was saponified by a mixture of 2 N aqueous NaOH and ethanol to give, after acidification, III (R = H). III (R = H) at 3.3 + 10-7 M in vitro enhanced cell differentiation-inducing activity of retinoic acid in human leukemia HL-60 cells by 14% (retinoic acid alone) to 76% (retinoic acid and the present compound) in an assay measuring degree of cell differentiation to granulocyte cells by reduction of nitrobluetetrazolium (NBT).

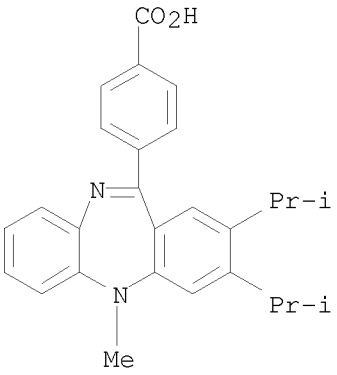
IT 172705-89-4P 188844-28-2P 188844-31-7P
188844-34-0P 188844-37-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (di)benzodiazepine, (di)benzothiazepine, and (di)benzoxazepine compds. potentiating biol. activities of retinoids)

RN 172705-89-4 CAPLUS

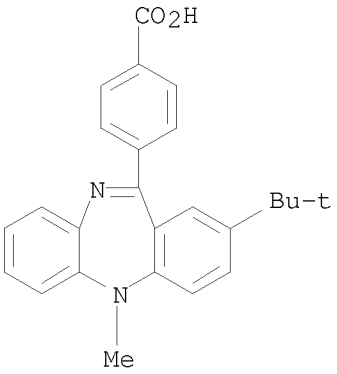
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



RN 188844-28-2 CAPLUS
CN Benzoic acid, 4-[5-methyl-2,3-bis(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)

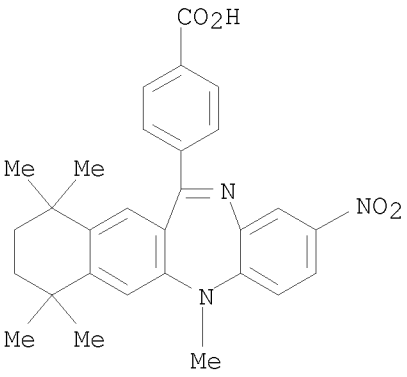


RN 188844-31-7 CAPLUS
CN Benzoic acid, 4-[2-(1,1-dimethylethyl)-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl]- (CA INDEX NAME)

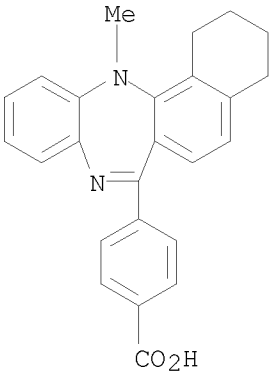


RN 188844-34-0 CAPLUS

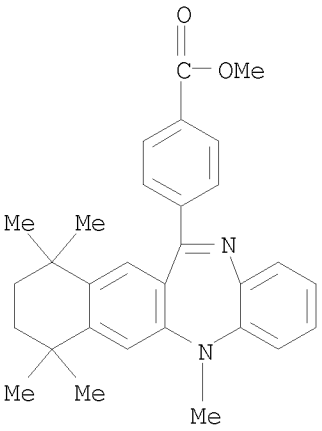
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



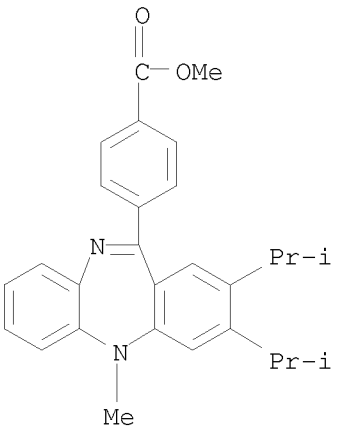
RN 188844-37-3 CAPLUS
CN Benzoic acid, 4-(2,3,4,13-tetrahydro-13-methyl-1H-benzo[b]naphtho[1,2-e][1,4]diazepin-7-yl)- (CA INDEX NAME)



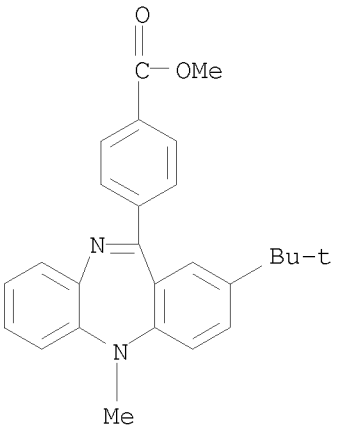
IT 188844-81-7P 188844-95-3P 188845-09-2P
188845-12-7P 188845-24-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (di)benzodiazepine, (di)benzothiazepine, and (di)benzoxazepine compds. potentiating biol. activities of retinoids)
RN 188844-81-7 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



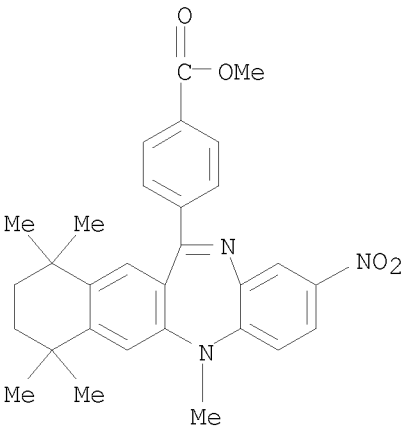
RN 188844-95-3 CAPLUS
CN Benzoic acid, 4-[5-methyl-2,3-bis(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepin-11-yl]-, methyl ester (CA INDEX NAME)



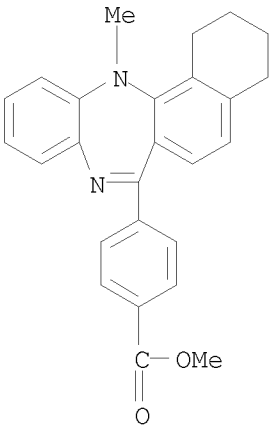
RN 188845-09-2 CAPLUS
CN Benzoic acid, 4-[2-(1,1-dimethylethyl)-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-yl]-, methyl ester (CA INDEX NAME)



RN 188845-12-7 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-2-nitro-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)-, methyl ester (CA INDEX NAME)



RN 188845-24-1 CAPLUS
CN Benzoic acid, 4-(2,3,4,13-tetrahydro-13-methyl-1H-benzo[b]naphtho[1,2-e][1,4]diazepin-7-yl)-, methyl ester (CA INDEX NAME)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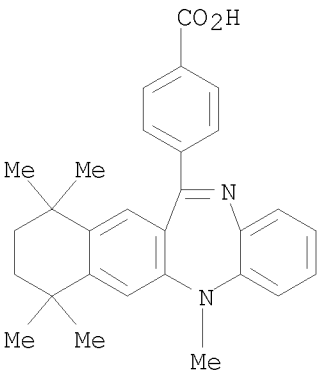
L25 ANSWER 46 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:274651 CAPLUS
DOCUMENT NUMBER: 127:13060
ORIGINAL REFERENCE NO.: 127:2515a,2518a
TITLE: Action mechanism of retinoid-synergistic dibenzodiazepines
AUTHOR(S): Umemiya, Hiroki; Kagechika, Hiroyuki; Fukasawa, Hiroshi; Kawachi, Emiko; Ebisawa, Masayuki; Hashimoto, Yuichi; Eisenmann, Ghislaine; Erb, Cathie; Pornon, Astrid; Chambon, Pierre; Gronemeyer, Hinrich; Shudo, Koichi
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, University of Tokyo, Bunkyo-ku, Tokyo, 113, Japan
SOURCE: Biochemical and Biophysical Research Communications (1997), 233(1), 121-125
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 4-[5H,2,3-(2,5-Dimethyl-2,5-hexano)-5-methyldibenzo[b,e][1,4]diazepin-11-yl]benzoic acid (HX600), as well as its oxa- (HX620) and thia- (HX630) analogs, enhanced the activity of retinoic acid and a receptor α (RARα)-selective agonist Am80 in HL-60 cell differentiation assays. HX600 synergizes with Am80 by binding to, and transactivating through, the RXR subunit of the RXR-RAR heterodimer. HX600 exhibited RXR pan-agonist activity in transient transfections with a DR1-based reporter gene and synergized with RA-bound RARα and RARβ in inducing transcription from a DR5-based reporter. In addition, all three compds. at high concns. acted as RAR pan-antagonists in stably transfected RAR "reporter cells". These efficient synergists bind only weakly with RXRs in vitro, suggesting that they are RXR-RAR heterodimer-selective activators. These HX retinoids exhibited dual functionality, since they affected signalling through both retinoid receptor families (RARs and RXRs).

IT 172705-89-4, HX600
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(action mechanism of retinoid-synergistic dibenzodiazepines)

RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)

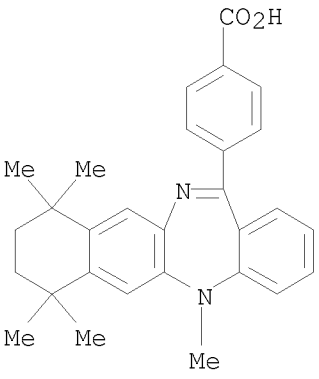


REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

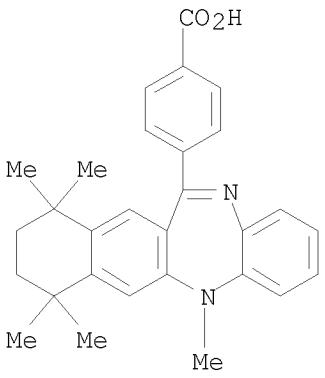
L25 ANSWER 47 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:143330 CAPLUS
DOCUMENT NUMBER: 126:246352
ORIGINAL REFERENCE NO.: 126:47479a,47482a
TITLE: Inhibition of IL-1-induced IL-6 production by synthetic retinoids
AUTHOR(S): Kagechika, Hiroyuki; Kawachi, Emiko; Fukasawa, Hiroshi; Saito, Go; Iwanami, Naoko; Umemiya, Hiroki; Hashimoto, Yuichi; Shudo, Koichi
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, University of Tokyo, Tokyo, 113, Japan
SOURCE: Biochemical and Biophysical Research Communications (1997), 231(2), 243-248
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of retinoids and retinoid antagonists on IL-6 production in MC3T3-E1 cells were investigated. None of the synthetic retinoids examined stimulated IL-6 production, but all of them strongly inhibited IL-6 production induced by mouse IL-1α. Their inhibitory activities correlated well with their differentiation-inducing activities in HL-60 assay or their binding affinities to nuclear retinoic acid receptors (RARs). Among three retinoid antagonists, two weak antagonists exhibited similar inhibition of mouse IL-1α-induced IL-6 production, whereas a potent retinoid antagonist, 4-(13H-10,11,12,13-tetrahydro-10,10,13,13,15-pentamethyl-dinaphtho[2,3-b][1,2-e]diazepin-7-yl)benzoic acid (LE540), enhanced IL-6 production under the same conditions.

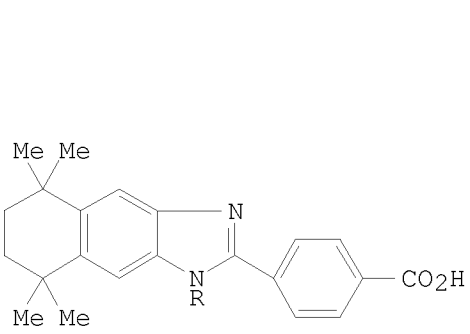
IT 155877-83-1, LE 135
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of IL-1-induced IL-6 production by synthetic retinoids and retinoid antagonists in relation to differentiation-inducing activity and retinoid receptor binding and structure)
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



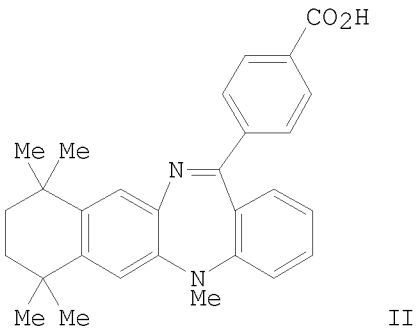
L25 ANSWER 48 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:959457 CAPLUS
DOCUMENT NUMBER: 124:75750
ORIGINAL REFERENCE NO.: 124:13833a,13836a
TITLE: Synergists for retinoid in cellular differentiation of human promyelocytic leukemia cells HL-60
AUTHOR(S): Umemiya, Hiroki; Kawachi, Emiko; Kagechika, Hiroyuki; Fukasawa, Hiroshi; Hashimoto, Yuichi; Shudo, Koichi
CORPORATE SOURCE: Fac. Pharmaceutical Sci., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1995), 43(10), 1827-9
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 4-[5H-2,3-(2,5-dimethyl-2,5-hexano)-5-methyldibenzo[b,e]diazepin-11-yl]benzoic acid (I) enhanced the differentiation-inducing activity of retinoic acid and of a synthetic retinoid Am80 toward human promyelocytic leukemia cells HL-60, although I alone did not induce differentiation. The synergistic effect of I on the activities of retinoids was also seen in suppression of proliferation of HL-60 cells.
IT 172705-89-4, HX 600
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synergists for retinoid in cellular differentiation of human promyelocytic leukemia cells HL-60)
RN 172705-89-4 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[b]naphtho[2,3-e][1,4]diazepin-12-yl)- (CA INDEX NAME)



L25 ANSWER 49 OF 49 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:435911 CAPLUS
DOCUMENT NUMBER: 121:35911
ORIGINAL REFERENCE NO.: 121:6651a,6654a
TITLE: Retinobenzoic Acids. 6. Retinoid Antagonists with a Heterocyclic Ring
AUTHOR(S): Eyrolles, Laurence; Kagechika, Hiroyuki; Kawachi, Emiko; Fukasawa, Hiroshi; Iijima, Tohru; Matsushima, Youko; Hashimoto, Yuichi; Shudo, Koichi
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, University of Tokyo, Tokyo, 113, Japan
SOURCE: Journal of Medicinal Chemistry (1994), 37(10), 1508-17
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

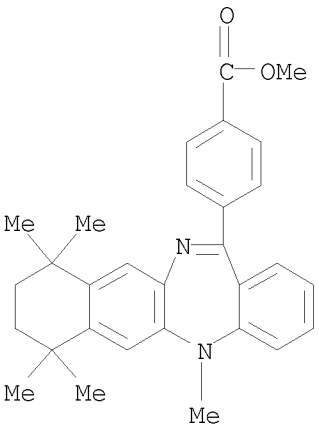


II

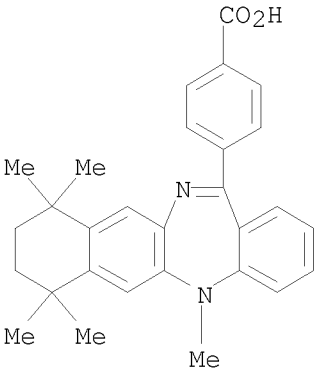
AB Several candidate retinoid antagonists were designed on the basis of the ligand superfamily concept and synthesized. Retinoidal activities of these benzimidazole and benzodiazepine derivs. were examined by assay of differentiation-inducing activity on human promyelocytic leukemia cell line HL-60. The benzimidazole derivs.I [R = H, Me, Et, CHMe2, CH2Ph, Ph] exhibited retinoidal activity, and the potency strongly depended on the bulkiness of the substituent. I [R = Ph, benzyl] lacked differentiation-inducing activity on HL-60 cells and acted as antagonists to the potent retinoid 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid (Am80). Among the compds. possessing a seven-membered heterocyclic ring as a linking group, 4-(5H-7,8,9,10-tetrahydro-5,7,7,10,10-pentamethylbenzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)benzoic acid (II) also exhibited the antagonistic activity. The binding abilities of these compds. to retinoic acid receptors α and β were consistent with their potency for the inhibition of HL-60 cell differentiation induced by the retinoid Am80.

IT 155877-82-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of benzonaphthodiazepinylbenzoate retinoid antagonists)
RN 155877-82-0 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-

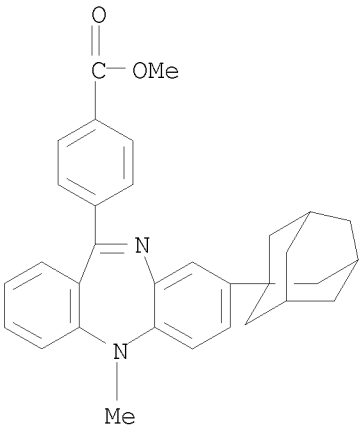
benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)-, methyl ester (CA INDEX NAME)



IT 155877-83-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and retinoid antagonist activity of)
RN 155877-83-1 CAPLUS
CN Benzoic acid, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5H-benzo[e]naphtho[2,3-b][1,4]diazepin-13-yl)- (CA INDEX NAME)



L23 ANSWER 13 OF 13 REGISTRY COPYRIGHT 2008 ACS on STN
RN 1025849-67-5 REGISTRY
ED Entered STN: 05 Jun 2008
CN Benzoic acid, 4-(5-methyl-8-tricyclo[3.3.1.13,7]dec-1-yl-5H-dibenzo[b,e][1,4]diazepin-11-yl)-, methyl ester (CA INDEX NAME)
MF C32 H32 N2 O2
SR Other Sources
Database: ChemSpider (ChemZoo, Inc.)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT